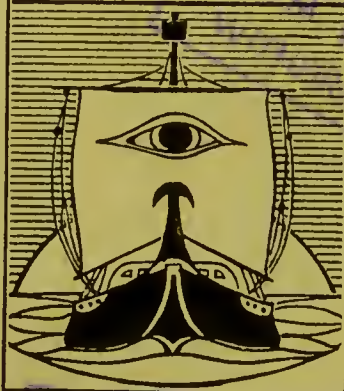


NOT TO BE TAKEN FROM THE LIBRARY

S. T. M. LIBRARY
WITHDRAWN
THE UNIVERSITY OF LIVERPOOL

LIBRARY OF THE
LIVERPOOL SCHOOL
OF TROPICAL
MEDICINE



S. T. M. LIBRARY
WITHDRAWN
LIBRARY
WITHDRAWN

PRESS MARK

Press Letter LO.AC. 2.5.
Shelf No.....
Book No.....

LSHTM



001130098X



With Col. J. G. ...
Royal Society, 1905
OFFICIAL COPY.

[All rights reserved.]

REPORTS
OF THE
SLEEPING SICKNESS COMMISSION
OF THE
ROYAL SOCIETY.

No. VI.

11. **Continuation Report on Sleeping Sickness in Uganda.** By Captain E. D. W. GREIG, I.M.S., and Lieutenant A. C. H. GRAY, R.A.M.C. (Sleeping Sickness Commission).
12. **Report on Sleeping Sickness in the Nile Valley.** By Captain E. D. W. GREIG, I.M.S.
13. **The Distribution of the Tsetse Flies** (*with Map*). By E. E. AUSTEN, F.Z.S.
14. **The Multiplication of the Trypanosoma Gambiense in the Alimentary Canal of Glossina Palpalis.** By Lieutenant A. C. H. GRAY, R.A.M.C., and Lieutenant F. M. G. TULLOCH, R.A.M.C.

LONDON :
PRINTED FOR HIS MAJESTY'S STATIONERY OFFICE,
BY HARRISON AND SONS, ST. MARTIN'S LANE,
PRINTERS IN ORDINARY TO HIS MAJESTY.

And to be purchased, either directly or through any Bookseller, from
WYMAN AND SONS, LTD., FETTER LANE, E.C.; or
OLIVER AND BOYD, EDINBURGH; or
E. PONSONBY, 116, GRAFTON STREET, DUBLIN.

1905.

Price Four Shillings and Sixpence.

AUGUST.



With Col. D. Bruce, D.S.O., M.C.

Royal Army Medical Corps

Milibank, S.W.

CONTINUATION REPORT

ON

SLEEPING SICKNESS IN UGANDA.

BY

CAPT. E. D. W. GREIG, I.M.S.

AND

LIEUT. A. C. H. GRAY, R.A.M.C.

(SLEEPING SICKNESS COMMISSION.)

LONDON :

PRINTED FOR HIS MAJESTY'S STATIONERY OFFICE,
BY HARRISON AND SONS, ST. MARTIN'S LANE,
PRINTERS IN ORDINARY TO HIS MAJESTY.

And to be purchased, either directly or through any Bookseller, from
WYMAN AND SONS, LTD., FETTER LANE, E.C.; or
OLIVER AND BOYD, EDINBURGH; or
E. PONSONBY, 116, GRAFTON STREET, DUBLIN.

1905.

Price Four Shillings and Sixpence.

AUGUST.

(Wt. 9387 1375 8 | 05—H & S 7390)

11.

CONTENTS.

	PAGE
Introductory	5
1-3. Lymphatic Glands in Sleeping Sickness	7
4. Blood in Sleeping Sickness	18
5. Cerebro-spinal Fluid in Sleeping Sickness	25
6-7. Bacterial Invasion in Sleeping Sickness	28
8. Relation of Trypanosoma Fever to Sleeping Sickness	39
9. Trypanosoma Experiments with Animals	73
10. Distribution of Sleeping Sickness and <i>Glossina Palpalis</i>	102
11. Fresh Fly (<i>Glossina Palpalis</i>) Trypanosoma	104
12. Other Varieties of Trypanosoma in Uganda	111
13. History and Distribution of these Trypanosomes... ..	111
14. Trypanosomes of Entebbe Ox, Jinja Cattle, Abyssinian and Entebbe Mules	112
15. Animal Experiments with these Trypanosomes	112
16. Are we Dealing with one or more than one Species?	193
17. Can the <i>Glossina Palpalis</i> convey these Trypanosomes?	197
18. Can other Biting Flies (Stomoxys) convey these ?	203
Appendix	209

LIST OF ILLUSTRATIONS.

1. Map of Distribution of *Glossina Palpalis* in Uganda (*see* p. 102).
2. Map of Distribution of Sleeping Sickness in Uganda (*see* p. 102).
3. Coloured Plate of Trypanosomes of "Jinja Cattle" Disease (*see* p. 112).
4. Coloured Plate of Trypanosomes of "Abyssinian" Disease (*see* p. 112).
5. Coloured Plate of Trypanosomes of "Mule" Disease (*see* p. 154).
6. Two Photographs of Arcadi, Case 69 ZN. (*see* p. 246).
7. Coloured Plate of Stomach of Case 69 Z.Q. (*see* page 266).
8. Mr. Austen's Map of Africa showing distribution of Tsetse Flies (*see* p. 283).

INTRODUCTORY.

SINCE the departure of Colonel D. Bruce, F.R.S., for England on August 28, 1903, the work of the Commission was carried on by Greig and Nabarro until November 20, 1903. On that date Dr. Nabarro left Entebbe for England. The work of the Commission was conducted by Captain Greig until he was joined on March 9, 1904, by Lieutenant A. C. H. Gray, R.A.M.C.

Captain Greig left Entebbe for England on November 15, *via* the Nile and Egypt.

This Continuation Report brings the work of the Commission up to the date of Greig's departure for England.

In this Report evidence is brought forward which affords additional proof of the correctness of the conclusions arrived at in the last Report. Further evidence is brought forward to show:—

1. That the disease is at first a specific polyadenitis caused by the *Trypanosoma gambiense*.
2. That in addition to enlargement of lymphatic glands the blood shows a constant lymphocytosis at all stages of the disease.
3. That Sleeping Sickness is the last stage of this disease, and is invariably fatal. It consists essentially in a polyadenitis plus signs and symptoms due to changes in the nervous system; the onset of these signs and symptoms synchronises with the entrance of the *Trypanosoma gambiense* into the lymph spaces of the nervous system; this is accompanied by a rise of the mononuclear elements in the cerebro-spinal fluid.
4. That the resistance of both men and monkeys to the *Trypanosoma gambiense*, as judged by the duration of the early stage, varies greatly, and probably a certain proportion, not yet exactly determined, acquire sufficient immunity to arrest the development of the disease at that stage.
5. That the action of arsenic *in vita* on the *Trypanosoma gambiense* is partial. It destroys a number of the trypanosomes, and probably these act as immunising agents. Its administration in the stage of polyadenitis tends to help the natural resistance to combat the disease.
6. That bacterial invasion, chiefly coccal, occurs in some cases, but only in the very last days of the sleeping sickness stage, and therefore cannot determine the onset of this phase of the malady.

7. That in addition to the *Trypanosoma gambiense*, other varieties of trypanosoma occur in Uganda which are pathogenic to animals.
8. That these trypanosomes differ entirely from *Trypanosoma gambiense* in morphology and animal reactions.
9. That one of these trypanosomes is probably identical with *Trypanosoma brucei*. The other two differ from it and are, provisionally, unclassified.
10. That these varieties of trypanosomes are conveyed from the sick to the healthy by the Uganda tsetse fly (*Glossina palpalis*) and not by other biting flies (*Stomoxys*).

The general situation as regards sleeping sickness in Uganda at the present time may be summed up as follows:—In the sleeping sickness areas from 50 per cent. to 75 per cent. of the inhabitants are in the stage of polyadenitis and are carrying on their ordinary work, because the disease at this stage produces few symptoms; but they are acting as reservoirs of the parasite, like the wild animals in the case of Nagana. It is this class of case that is specially liable to infect “clean” fly belts. The after history of these early cases, so far as we have observed up to the present, is as follows:—(1) That they may terminate fatally, either (*a*) by passing into the stage of sleeping sickness, which is the most frequent and usual; (*b*) through some intercurrent affections, particularly pneumonia. In this connection it is interesting to note that Dr. Albert Cook has observed that the admissions for pneumonia to the C.M.S. Hospital, Mengo, have risen markedly within the last two years. (2) That they remain in good health for long periods, indicating that at least a “tolerance” to the parasite has been acquired. The question then arises: will any of these individuals acquire sufficient immunity to destroy the parasite at this stage? Can they in fact become “salted”? and further, can this immunity by any means be artificially increased?

From reports just received there is reason to believe that the hitherto “clean” fly belt on Lake Albert and the Nile has become infected. The suspected district is Bugungu near Fajao, where the *Glossina palpalis* was obtained last year. The subject is being further investigated. If the disease is sleeping sickness, the infection must have been either carried across Unyoro from Uganda or travelled along the Nile from Usoga. As the *Glossina palpalis* has been found at Nimule and probably exists north of that, the disease will involve an extensive tract of fresh country.*

* The most recent Reports confirm the original information that sleeping sickness has broken out in this area. Captain Greig is proceeding to England, *via* the Nile and Egypt, in order to investigate this outbreak and also to determine the presence or absence of *Glossina palpalis* and trypanosomiasis in Egypt. The results of this expedition will be reported on its completion, *vide* Report 12 (p. 273).

A feature in the morbid anatomy of sleeping sickness, to which attention has not previously been directed, is a curious condition found in the stomach. In a number of cases the organ was found to contain a quantity of dark, semi-fluid material. The mucous membrane showed a remarkable alteration; it was studded with areas of varying size, having a dark centre and a light red periphery. They were most numerous towards the pyloric orifice, *vide* Plate 7, p. 266. On microscopical examination they were seen to be petechial hæmorrhages into the mucous membrane, which had broken down and formed superficial ulcers. No ova of *Bilharzia* were seen in the scrapings. A full account is given in the histories of the cases recorded in the Appendix. In all cases in which the stomach was inspected this condition was met with. The condition is comparable with the petechial hæmorrhages met with under the endo- and epicardium of the heart in trypanosoma infections.

The members of the Commission take this opportunity of expressing their most sincere thanks to Colonel Hayes-Sadler, C.B., His Majesty's Commissioner and Consul-General, Uganda, for his constant kindness and encouragement; to Mr. George Wilson, C.B., His Majesty's Acting Commissioner, Uganda, for helping forward the work of the Commission; to Mr. W. Grant, C.M.G., for his co-operation in the work in Busoga; to Major Will, P.M.O., for facilities afforded; to Dr. Moffat, C.M.G., for his valuable help and advice; to the Bishops of the various churches and their missionaries. We desire to express our best thanks to Professor Ray Lankester, the Director, to Mr. Austen, the entomologist, and Mr. Jeffrey Bell, of the British Museum (Natural History), for their kindness in examining and reporting on specimens sent; lastly, to Mrs. Bruce for several very accurate coloured drawings, and to Colonel Bruce, F.R.S., whose co-operation in England has been of the greatest value to us here.

1. *The lymphatic glands of every case of sleeping sickness are enlarged and the juice taken by puncture during life contains many active trypanosomes and also disintegrating forms.*

Every case of sleeping sickness here has shown enlargement of the lymphatic glands. The enlargement of the femoral, inguinal, axillary and superficial cervical glands can, during life, be readily determined, and after death the abdominal, thoracic and deep cervical.

In the *Proceedings of the Royal Society* for May, 1904, it was pointed out that the juice of the lymphatic glands, especially the posterior cervical glands, contains many active trypanosomes in all cases and at all stages of sleeping sickness.

Some of the juice can easily be obtained by puncturing a superficial gland in the posterior triangle of the neck with a hypodermic needle and sucking it into the needle by means of a syringe. The drop is then blown out on to a slide, covered with a cover glass and examined under a low power, 150 to

200 diameters of the microscope—Zeiss 16 mm. objective and Nos. 12 or 18 eyepiece. The trypanosomes are numerous in the juice and are readily found after a short search. In stained preparations, in addition to well-formed trypanosomes, there exist a considerable number of disintegrating forms, suggesting that destruction of trypanosomes takes place in the glands. Similar preparations from a drop of peripheral blood were prepared and examined at the same time, but a prolonged search in the majority of cases failed to discover the presence of trypanosomes.

A practical outcome of these observations will be, that the recognition of sleeping sickness in its earliest stages will be a matter of easy accomplishment: the enlargement of the superficial lymphatic glands presents a sign which will arrest the attention of the observer, and the determination, by the above method, of the presence of trypanosomes in them can be very simply carried out.

The trypanosomes are present in small numbers in the peripheral blood, but from time to time an increase in their numbers takes place. This increase suggests that an occasional overflow from the glands, to which they are chiefly confined, takes place. The trypanosomes are sometimes more numerous in the blood taken at night time.

The juice of the gland was found sterile and free from streptococci even at a late stage of the disease. As will be shown later, the streptococcic invasion occurs only when the patient is moribund.

A point of interest, in connection with glandular enlargements due to *Trypanosoma gambiense*, is that in monkeys which have been inoculated with the trypanosoma, glandular enlargement is not so marked as in man, the parasite being found more frequently in the blood of monkeys, the disease being in monkeys more a blood one than is the case in man. This absence of gland enlargement in monkeys might explain why the mononuclear exudation which is present in all cases of sleeping sickness (Mott) is not also seen in monkeys.

The following table shows the result of these enumerations at all stages of the disease in cases of sleeping sickness:—

RESULT OF THIS PROCEDURE IN 62 CASES.

Date. 1904.	No.	Name.	Age.	Sex.	Stage of disease.	Situation of glands.	Parasites in lymph juice.		Parasites in peripheral blood.		
							Strepto.	Tryp.	Filar.	Malar.	Tryp.
March 14	1	Sempagana ...	10	M.	2nd	R. post. triangle ...	Absent	Present	Present	Absent	Absent
" 15	2	Sabakaki ...	12	"	2nd	R. post. triangle ...	"	"	"	"	"
" 16	3	Naguta ...	25	F.	1st	L. ant. triangle ...	"	"	Absent	"	"
" 17	4	Zeridan ...	10	M.	3rd	L. post. triangle ...	"	"	"	"	"
" 19	5	Abimerika ...	25	"	2nd	L. femoral	"
" 21	6	Jordan Murjan	35	"	1st	R. post. triangle ...	Absent	"	Absent	Absent	Absent
" 22	7	Zrigoa ...	20	"	3rd	L. femoral	"
" 23	8	Erya ...	25	"	1st	R. post. triangle ...	Absent	"	Present	Present	Present
" 26	9	Wasiwa ...	18	"	2nd	R. femoral	"	Present	Present	Present
" 27	10	Nasanera ...	25	"	3rd	L. post. triangle ...	Absent	"	Present	Present	Present
" 28	11	Kirongo ...	35	"	2nd	L. post. triangle	"
" 29	12	Tabula ...	26	"	Early stage	R. femoral ...	Absent	"	Absent	Absent	Absent
" 30	13	Bara Risgalla	36	"	"	R. post. triangle	"
						L. femoral ...	"	"	"	"	"
							...	Absent

RESULT OF THIS PROCEDURE IN 62 CASES—continued.

Date 1904.	No.	Name.	Age.	Sex.	Stage of disease.	Situation of glands.	Parasites in lymph juice.		Parasites in peripheral blood.		
							Strepto.	Tryp.	Filar.	Malar.	Tryp.
April	4	Karala Barigi	25	M.	Early stage	R. post. triangle ...	Absent	Present	Absent	Absent	Absent
"	5	Kumsasabba	26	"	"	L. post. triangle ...	"	"	"	"	"
"	9	Zmiwanguiza	20	"	3rd	L. post. triangle ...	"	"	"	"	"
"	11	Yerimya	30	"	2nd	L. post. triangle ...	"	"	Present	"	"
"	13	Danielli	20	"	1st	L. post. triangle ...	"	"	Absent	"	"
"	13	Gangabudi	35	"	3rd	R. ant. triangle ...	"	"	"	"	"
"	13	Numa	25	"	1st	L. post. triangle ...	"	"	"	"	"
"	25	Sumani	18	"	3rd	R. ant. triangle ...	"	"	"	"	"
"	28	Musaja Kangoa	35	"	2nd	R. and L. post. tri- angles	"	"	Present	"	"
May	2	Daudi Makasa	18	"	1st	R. and L. post. tri- angles	"	"	"	"	"
"	3	Arena	16	F.	"	R. and L. post. tri- angles	"	"	Absent	"	"
"	4	Kaboa Jongira	14	M.	"	R. post. triangle ...	"	"	"	"	"
"	5	Hamisi	14	"	"	L. post. triangle ...	"	"	Present	Present	Present
"	6	Msoqe	16	"	"	R. post. triangle ...	"	"	Absent	Absent	Absent
"	10	Arisati	7	F.	"	R. and L. post. tri- angles	"	"	"	"	"
"	11	Mundu	38	M.	2nd	R. ant. triangle ...	"	"	"	"	"
"	14	Juma...	35	"	1st	R. ant. triangle ...	"	"	"	"	"
"	17	Arcada	25	"	2nd	R. ant. triangle ...	"	"	"	"	Present

"	18	32	Simoni	...	20	"	2nd	R. post. triangle ...	"	"	"	Absent
"	19	33	Yosuwa	Bazambude	20	"	1st	L. post. triangle ...	"	"	"	"
"	20	34	Nuwa	Kakabange	31	"	2nd	L. post. triangle ...	"	"	"	Present
"	21	35	Lotone	...	40	"	3rd	R. femoral	"	"	"	Absent
"	23	36	Zakayo	...	15	"	2nd	R. post. triangle ...	"	"	Present	"
"	25	37	Asumani	...	14	"	3rd	L. post. triangle ...	"	"	Absent	"
"	26	38	Abrahim	...	18	"	2nd	R. ant. triangle	"	"	"	"
"	27	39	Labaka	...	20	F.	1st	L. post. triangle	"	"	"	"
"	29	40	Zaka	25	M.	Early stage	R. post. triangle ...	"	"	"	Present
"	29	41	Dona	25	"	"	L. post. triangle	"	"	Present	Absent
June	1	42	Wabasa	Abamullah	35	F.	3rd	L. post. triangle ...	"	"	"	"
"	3	43	Bafrawalla	...	18	M.	"	L. post. triangle	"	"	"	"
"	6	44	Tenwa	...	25	"	Early stage	L. post. triangle ...	"	"	"	Present
"	6	45	Kitsame	...	26	"	"	L. post. triangle	"	"	"	"
"	12	46	Manawa	...	25	"	"	L. post. triangle	"	"	"	"
July	6	47	Nkola	...	25	"	"	L. post. triangle	"	"	"	Absent
"	6	48	Suedi...	...	30	"	2nd	R. post. triangle	"	"	"	"
"	9	49	Mundu	...	25	"	Early stage	R. post. triangle ...	"	"	"	Present
"	11	50	Zimageza	...	14	"	2nd	L. post. triangle	"	"	"	"
"	13	51	Nematude	...	20	F.	Early stage	L. post. triangle	"	"	"	"
August	10	52	Kasemota	...	25	M.	"	R. post. triangle	"	"	"	Absent
"	15	53	Alyabu	Mustafia	25	"	2nd	R. post. triangle	"	"	"	Present
"	17	54	Sururu	Mzee	25	"	3rd	L. post. triangle	"	"	"	Absent
"	24	55	Asha	16	F.	"	R. post. triangle	"	"	"	"
Sept.	20	56	Redza	...	14	M.	Early stage	L. post. triangle ...	"	"	"	Not observed
"	24	57	Omera	...	14	"	"	L. post. triangle	"	"	observed	Absent
"	26	58	Matiansi	...	22	"	1st	L. post. triangle	"	"	Not	Not
"	27	59	Sabugao	...	22	"	"	L. post. triangle	"	"	observed	observed
Oct.	13	60	Marco	Lukoma	35	"	Early stage	R. post. triangle	"	"	Absent	Absent
"	19	61	Mabruki	...	30	"	2nd	L. post. triangle	"	"	Not	Not
"	26	62	Petro	...	25	"	1st	L. post. triangle	"	"	observed	observed

2. *The lymphatic glands of cases of so-called "Trypanosoma Fever" are enlarged and the juice taken by puncture during life contains active and disintegrating trypanosomes.*

The early cases of trypanosomiasis examined here have all presented enlargement of the lymphatic glands and on puncturing them, active trypanosomes have been readily found. At this stage of the disease the condition is essentially a polyadenitis.

Sleeping sickness is this specific polyadenitis with sigus, originating in a derangement of the nervous system due to changes produced by the presence of the parasites there, superadded.

The occurrence of enlargement of the lymphatic glands with the presence of trypanosomes in number in both early cases of trypanosomiasis and sleeping sickness affords additional evidence in favour of the unity of the two conditions.

The natives themselves are alive to the fact that, when the glands in the neck become enlarged, they will, sooner or later, pass into the stage of sleeping sickness, and their custom is, then, to eat up their live stock, goats, chickens, &c.

In the above table the results of the examination of these early cases are given.

From the above observations the next question arises—

3. *What is the incidence of enlargement of lymphatic glands amongst the general population?*

It seemed important to test the above observations on a large scale. If trypanosomiasis causes adenitis, cases of enlargement of glands should be more numerous in the sleeping sickness areas than in the non-sleeping sickness areas. The incidence of gland enlargement in the sleeping sickness areas would be a gauge of the incidence of trypanosomes in the general population in sleeping sickness areas, because the majority of cases coming from sleeping sickness areas with enlarged glands have on examination showed the presence of trypanosomes in the glands.

In the sleeping sickness areas the incidence was obtained by the help of the Rev. H. T. C. Weatherhead, B.A., in the islands of Sese and Kome.

The results of these enumerations are given in the following lists. These have been given in full, and as each individual in these sleeping sickness areas has been accurately located, they will be of importance in following out the after history of the patients:—

INCIDENCE OF GLAND ENLARGEMENT OF GENERAL POPULATION.

A. *Sleeping Sickness Area—Sese Islands.*

Date. 1904.	Name.	Age.	Sex.	District.	Shamba.	Name of Chief.	Glands of Neck.
May 27	Yeremiya Mutanulwa	30	M.	Bukasa	Embuga	Kaganda	-
"	Labahi Bugutana	25	"	"	"	"	+
"	Zanala...	20	"	"	"	"	-
"	Lukusa...	55	"	"	Buzingo	"	+
"	Lwemba	40	"	"	Embuga	"	-
"	Baswezi	50	"	"	Buzingo	"	+
"	Sabakaki	16	"	Mengo (Buganda)	Lubaga	Sezi ...	-
"	Petero Kukulubwa	40	"	Bukasa	Embuga	Kaganda	+
"	Wasuzi...	30	"	"	"	"	+
"	Daki ...	13	"	"	"	"	+
"	Mukasa	15	"	Bubeke	Bulega	Katonya	-
"	Mukwaya	14	"	"	"	"	-
"	Simeoni Nsiyaleta	22	"	Bukasa	Embuga	Kaganda	-
"	Tonasi Bajira...	28	"	"	"	"	-
"	Sitefans Tefe	16	"	"	"	"	+
"	Tito Zirimeniya	12	"	"	"	"	-
"	Kivamengo	11	"	"	"	"	+
"	Myangubi	11	"	"	"	"	+
"	Kabanda	11	"	"	"	"	-
"	Tazerika	13	"	"	"	"	-
"	Eriga Bagalisa	20	"	"	"	"	+
"	Kakwenda	35	"	"	"	"	-

INCIDENCE OF GLAND ENLARGEMENT OF GENERAL POPULATION—*continued.*

Date. 1904.	Name.	Age.	Sex.	District.	Shamba.	Name of Chief	Glands of Neck.
May 27	Kagwaga ...	55	M.	Bukasa	Embuga	Kaganda	-
"	Sebugawo ...	45	"	"	Buwazi	"	+
"	Luvokwaya ...	48	"	"	"	"	+
June 2	Mika Mbujeramba	20	"	Bugela	Kibanga	Church	-
"	Takiko Kitanze	25	"	"	"	"	-
"	Zakayo Mulwanji	28	"	Kome	Buve ...	"	+
"	Kezekiya Muganda	28	"	Bukasa	Mpata	Kaganda	-
"	Abiri Mukubansi	30	"	"	Embuga	"	+
"	Enoka Kubolikoza	23	"	Bugala	Kibanga	Church	+
"	Lebeka...	30	F.	Bagale	Kibanza	Lukanga Church	+
"	Daudi Kabimula	30	M.	"	"	"	+
"	Zekaligo Bakiku	32	"	"	Church	"	+
"	Ibalaimu Alideki	30	"	Bufunira	"	"	+
"	Gakobo Malikan	30	"	Bubeke	"	Katonya	-
"	Siva Semuswbwa	40	"	Bukasa	Buwanga	Kaganda	+
"	Nawa Musalala	28	"	Bugala	Church	Church	+
"	Kezekiya Yetokira	30	"	Buninga	Kasayi	Sewoya	+
June 4	Zamala ...	30	"	Lujabwa	Lujabwa	Semukade	-
"	Isaka Kawabwe	40	"	Bugala	Bugala	Kweba	+
"	Meseka Kibira	40	"	Busi ...	Bumisa	Mugema	-
"	Nsika ...	20	"	Bubembe	Bubembe	Chagu...	-
"	Nekemya Kalaban Jake	25	"	Bulima	Bwendero	Serninaga	+
"	Pasibye ...	40	"	Bafumira	Bafumira	Namumba	+
"	Namabiga ...	55	"	Buvu ...	Buwanga	Kanu Musaka	+

"	Gauawula	40	"	Bubeke	...	Kaude	...	Sabagabo	...	-
"	Sempagama	35	"	Buninga	...	Bugoye	...	Sewoya	...	+
"	Eria Byasi	30	"	Bugala	...	Church	...	Church	...	-
"	Mbageramula...	25	"	Bugale	...	"	...	"	...	+
"	Weraga	25	"	"	...	"	...	"	...	+
"	Semu Tagurisiza	25	"	"	...	"	...	"	...	+
"	Mbugeramula...	25	"	"	...	"	...	"	...	+
"	Petero Balimuta	25	"	"	...	"	...	"	...	+
"	Erasito Weraga	23	"	"	...	"	...	"	...	-
"	Yoveri Sebagoti	30	"	"	...	"	...	"	...	-
"	Kapelaga	23	"	"	...	"	...	"	...	-
"	Mirika wa Muzungu	35	F.	"	...	"	...	"	...	-
"	Ketula	17	"	"	...	"	...	"	...	-
"	Ana	19	"	"	...	"	...	"	...	+
"	Foesi	14	"	"	...	"	...	"	...	-
"	Emike	15	"	"	...	"	...	"	...	+
"	Kala	11	"	"	...	"	...	"	...	-
"	Amaziya	15	"	"	...	"	...	"	...	+

A. *Sleeping Sickness Area—Kome Island.*

June 25	Aloni Mukasa...	...	26	M.	Kome	Buwe...	Church	-
"	Ibulaimu Kigwana	...	35	"	"	Busaka	Malaki	-
"	Kamu Wallabye	...	35	"	"	Mubembe	Timotco	Sabadago	...	-
"	Yona Kidolime	...	25	"	"	Buwe...	Church	+
"	Zakaliya Bazironda	...	30	"	"	Ngaga	Kiranza	-
"	Leubeni Wakalo	...	30	"	"	Buwe...	Church	+
"	Muva wala	...	28	"	"	Busanga	Sekoba	-
"	Tebampirawbwe	...	25	F.	"	Buwe...	Church	+
"	Eduwadi Kiribwa	...	25	M.	"	"	"	+

INCIDENCE OF GLAND ENLARGEMENT OF GENERAL POPULATION—*continued.*

Date. 1904.	Name.	Age.	Sex.	District.	Shamba.	Name of Chief.	Glands of Neck.
June 25	Zakaliya Luanga	...	M.	Kome	Bajo ...	Zakalia Nanganga ...	-
"	Yonasuni Batirya	...	"	Nsazi...	Tabaliro	Serinya ...	-
"	Kipanda	...	"	Kome	Sama...	Mwambi ...	+
"	Bakayana	...	"	"	"	"	+
"	Eriya Kwabo	...	"	"	"	"	-
"	Kalibwani	...	"	"	Mubembe	Sabadago	+
"	Kiranze	...	"	"	Ngaga	Kiranze (himself)	-
"	Nantagya	...	"	"	Sama ...	Mwambi ...	+
"	Kiwuja...	...	"	"	"	"	+
"	Malakufana	...	"	"	"	"	+
"	Muluku	...	"	"	Mubembe	Sabadago	-
"	Zirigwa	...	"	"	Kabangala	Kipanda	+
"	Wakigo	...	"	"	Basanga	Sekoba	+
"	Mukubampanga	...	"	"	Kabangala	Kipanda	+
"	Mutekanga	...	"	"	Sama...	Mwambi ...	+
"	Kwatabaliawo...	...	"	"	Bugombe	Mukusu	-
"	Kapere...	...	"	"	"	"	+
"	Bazitye...	...	"	"	Kituza	Walagana	-
"	Banaleka	...	"	"	Kabembe	(Himself)	+
"	Katuntu	...	"	"	Sama...	Mwambi	-
"	Swabidere	...	"	"	Sese ...	Sekulu	-
"	Kibadu...	...	"	Swaji...	Busaka	Malaki	-
"	Wakigeri	...	"	Kome	Sama ...	Mwambi	-
"	Sabakaki	...	"	"	"	"	+

Examination of population of "B. Non-Sleeping Sickness Areas," showed that the incidence of gland enlargement was low.

4. *Lymphocytosis occurs in all cases of sleeping sickness.*

Enlargement of lymphatic glands being a constant feature in sleeping sickness, it was a matter of importance to determine whether the lymphocytes in the blood show an increase in numbers. This point is of interest further, because the most constant lesion found in the nervous system of sleeping sickness cases is an accumulation of cells of this nature in the perivascular lymph spaces.

In uncomplicated cases of sleeping sickness anæmia does not occur, the number of the red cells and the percentage of hæmoglobin being normal. Towards the end, in a certain proportion of cases, the number of red cells, the percentage of hæmoglobin and the specific gravity rise above the normal. These cases did not present any signs of cyanosis. The examination of the bone marrow in one of these cases showed a very large number of nucleated red cells, chiefly normo-blastic, but some megaloblasts were also present.

Mast cells were present in the blood of all cases to the extent of about 1 per cent.

The eosinophiles, also, form a higher proportion of the leucocytes than is normally met with.

The examination of the blood was made by means of a Thoma-Zeiss blood counting apparatus and a Gowers' hæmoglobinometer.

It was also found that the trypanosomes were more numerous in the blood at night time.

The following table shows the result of the enumeration of the blood cells and the percentage of hæmoglobin in 57 cases of sleeping sickness:—

RESULTS OF ENUMERATION OF BLOOD CORPUSCLES IN ABOVE CASES.

Date. 1904.	No.	Name.	Age.	Sex.	Stage of disease.	R.B.C's.	W.B.C's.	Percentages.				Hb. Per cent.
								P.N.	S.M.	L.M.	E.	
March 16	1	Sempagama	10	M.	2nd	53	33	14
June 2	"	"	"	"	3rd	4,340,000	8,750	26	52	22	0	72
" 5	"	"	"	"	...	4,400,000	10,000	33	45	19	3	72
" 15	"	"	"	"	...	3,600,000	74,680	42	43	15	0	70
March 16	2	Sabakaki	12	M.	2nd	32	37	31
June 5	"	"	"	"	3rd	3,900,000	6,800	57	34	9	...	68
March 16	3	Naguta	25	F.	1st	...	7,500	54	28	18	0	...
" 17	4	Zeridan	10	M.	3rd	...	15,000	45	39	14	2	...
" 18	5	Abimerika	25	M.	2nd	...	8,600	50	27	13	10	...
April 11	"	"	"	"	...	5,200,000	15,000	22	58	6	14	...
" 21	"	"	"	"	...	5,300,000	13,900	29	48	15	13	84
May 10	"	"	"	"	...	5,000,000	13,700	24	25	43	8	90
" 31	"	"	"	"	...	5,000,000	9,370	35	21	28	16	80
June 4	"	"	"	"	...	5,300,000	10,000	32	27	38	3	90
March 21	6	Jordan Murjan	35	M.	1st	...	6,560	52	30	13	5	...
June 7	"	"	"	"	...	4,000,000	9,400	52	27	17	4	...
March 22	7	Zrigoa	20	M.	3rd	...	9,060	53	37	10	0	...

RESULTS OF ENUMERATION OF BLOOD CORPUSCLES IN ABOVE CASES—continued.

Date. 1904.	No.	Name.	Age.	Sex.	Stage of disease.	R.B.C's.	W.B.C's.	Percentages.				Hb. Per cent.
								P.N.	S.M.	L.M.	E.	
March 23	8	Erya	1st	...	10,900	46	34	18	2	...
" 27	9	Wasiwa	2nd	...	13,400	49	29	8	14	...
April 19	"	"	18	M.	...	5,300,000	11,200	33	49	9	10	...
June 8	"	"	"	"	...	5,500,000	10,300	40	15	8	0	94
" 30	"	"	"	"	...	5,500,000	11,200	48	44	4	4	92
July 15	"	"	"	"	3rd	5,700,000	7,800	52	31	16	1	95
March 28	10	Nasanenni	3rd	...	16,500	38	48	12	2	...
" 28	11	Kirongo	2nd	...	6,400	51	35	10	4	...
April 11	"	"	35	M.	"	5,200,000	7,800	42	49	5	4	...
" 25	"	"	"	"	"	4,900,000	17,800	25	50	17	8	82
June 14	"	"	"	"	"	4,400,000	16,200	30	41	15	14	80
March 28	12	Tabula	Early stage	...	6,800	37	38	25	1	...
June 4	"	"	...	"	"	4,200,000	9,300	40	40	17	3	80
" 27	"	"	"	"	"	4,400,000	18,700	68
March 30	13	Bara Risgallah	Early stage	...	6,870	59	29	11	1	...
April 27	"	"	"	"	"	4,500,000	6,200	69	23	8	0	...
" 4	14	Karala Barigi	Early stage	...	22,500	53	32	10	5	...

"	5	15	Kumsarsabba	26	M.	Early stage	...	10,900	48	42	9	1	...
"	9	16	Zimwanguyza	20	M.	3rd	...	9,300	50	40	9	0	...
"	20	"	"	"	"	"	4,200,000	8,000	57	31	12	0	65
"	11	17	Yerinya	30	M.	2nd	4,500,000	7,800	42	49	5	4	...
"	19	"	"	"	"	"	5,500,000	11,200	33	49	9	10	...
"	28	"	"	"	"	"	5,300,000	9,060	35	47	16	2	85
"	13	18	Danielli	20	M.	1st	No observations.						
"	13	19	Gangabuda	35	M.	3rd	"	"	"	"	"	"	"
"	13	20	Johanna Numa	25	M.	1st	"	"	"	"	"	"	"
"	25	21	Sumani	18	M.	3rd	4,400,000	10,300	23	44	23	10	78
May	9	"	"	"	"	"	4,600,000	7,500	45	25	16	14	75
April	28	22	Musaja Kangow	35	M.	2nd	4,500,000	14,000	30	38	30	2	80
"	30	23	Daudi Mukasa	18	M.	1st	4,500,000	12,200	24	27	26	23	76
May	3	24	Arena	16	F.	1st	5,000,000	14,060	58	29	13	...	76
"	4	25	Kaba Jongira	14	M.	1st	5,000,000	14,300	30	33	19	18	90
"	5	26	Hamisi	14	M.	2nd	3,800,000	13,700	52	27	16	5	64
"	16	"	"	"	"	"	4,000,000	5,300	35	32	28	5	60
"	19	"	"	"	"	"	...	8,740	31	37	22	10	...
June	16	"	"	"	"	"	5,200,000	13,000	50	34	11	5	78
"	22	"	"	"	"	"	49	36	12	3	...
July	12	"	"	"	"	"	5,000,000	18,000	54	32	13	1	78

RESULTS OF ENUMERATION OF BLOOD CORPUSCLES IN ABOVE CASES—continued.

Date. 1904.	No.	Name.	Age.	Sex.	Stage of disease.	R.B.C.s	W.B.C's.	Percentages.				Hb. Per cent.
								P.N.	S.M.	L.M.	E.	
July 20	26	Hamisi ...	14	M.	3rd	5,400,000	38,100	65	24	11	...	84
May 6	27	Msoqe ...	16	M.	1st	4,050,000	9,060	49	17	25	9	75
" 10	28	Arisati ...	7	F.	1st	4,400,000	6,100	37	32	23	8	55
" 10	29	Mundu ...	38	M.	2nd	5,000,000	9,500	23	41	25	10	80
" 14	30	Juma ...	25	M.	1st	5,200,000	11,800	31	35	24	10	90
June 14	"	"	"	5,300,000	11,800	23	52	10	15	90
May 17	31	Arcadi ...	25	M.	2nd	5,100,000	17,000	35	34	29	2	84
July 14	"	" ...	"	"	3rd	5,900,000	13,750	54	30	9	...	100
" 15	"	" ...	"	"	"	6,000,000	14,800	46	36	11	7	100
" 19	"	" ...	"	"	"	6,000,000	12,500	55	33	9	3	102
" 21	"	" ...	"	"	"	6,020,000	14,300	50	43	5	2	102
" 18	32	Simeoni ...	20	M.	2nd	4,250,000	7,200	41	35	17	7	82
" 19	33	Yosuwa Basambude	20	M.	1st	4,600,000	6,800	46	28	23	3	86
" 20	34	Nuwa Kikabange	31	M.	2nd	4,750,000	16,000	29	38	30	3	66

"	21	35	Lotone	40	M.	3rd	2,600,000	6,800	60	23	14	3	35
"	23	36	Zakayo	15	M.	2nd	3,800,000	20,300	30	40	18	12	70
"	25	37	Asumani	14	M.	3rd	4,400,000	13,700	28	19	19	34	80
June 19	"	"	"	"	"	"	5,000,000	13,700	33	35	10	22	85
May 26	38	38	Abraham	18	M.	2nd	4,000,000	22,200	28	51	17	6	82
"	29	39	Labaka	20	F.	1st	41	32	18	9	...
June 18	"	"	"	"	"	"	5,300,000	9,700	39	46	7	8	90
May 29	40	40	Zaka	25	M.	Early stage	5,200,000	9,370	35	48	13	4	95
"	29	41	Dona	25	M.	Early stage	4,500,000	13,700	30	38	24	8	82
June 1	21	42	Wabasa Abamullah	35	M.	3rd	4,350,000	10,900	62	16	11	11	70
"	20	"	"	"	"	"	4,500,000	8,750	48	32	11	9	82
"	3	43	Bafrawalla	18	M.	3rd	5,400,000	11,250	40	36	21	3	90
"	20	"	"	"	"	"	5,000,000	8,000	36	51	11	2	74
"	7	44	Tenwa	25	M.	Early stage	3,700,000	6,000	38	46	13	3	66
July 11	"	"	"	"	"	"	4,000,000	6,850	30	64	3	3	68
"	17	"	"	"	"	"	4,300,000	6,600	14	69	9	8	74
June 7	7	45	Kitsame	26	M.	Early stage	4,800,000	12,500	47	30	21	2	80
July 8	"	"	"	"	"	"	4,200,000	3,800	25	61	2	12	72
"	17	"	"	"	"	"	4,900,000	5,800	20	58	13	9	80
June 12	12	46	Manawa	25	M.	Early stage	4,650,000	13,120	33	28	30	9	6
July 10	"	"	"	"	"	"	4,800,000	11,870	33	41	18	8	78
"	17	"	"	"	"	"	4,600,000	9,100	28	63	6	3	80

RESULTS OF ENUMERATION OF BLOOD CORPUSCLES IN ABOVE CASES--continued.

Date. 1904.	No.	Name.	Age.	Sex.	Stage of disease.	R.B.C's.	W.B.C's.	Percentages.				Hb. Per cent.
								P.N.	S.M.	L.M.	E.	
July 6	47	Nkolo	25	M.	Early stage	5,000,000	15,000	37	37	8	18	72
" 6	48	Suedi	30	M.	2nd	4,000,000	7,500	41	44	8	7	70
" 9	49	Mfoudu	25	M.	Early stage	5,200,000	8,700	47	38	5	10	80
" 12	"	"	"	"	"	5,100,000	9,000	42	40	6	12	86
" 17	"	"	"	"	"	5,130,000	10,000	32	48	8	12	89
" 11	50	Zemageza	14	M.	2nd	5,000,000	10,900	52	28	18	2	88
" 19	"	"	"	"	"	5,000,000	11,800	40	46	13	1	90
" 13	51	Namutide	20	F.	Early stage	4,400,000	15,000	33	40	7	20	78
" 15	"	"	"	"	"	4,500,000	10,000	26	49	9	16	76
Aug. 4	"	"	"	"	"	4,350,000	7,500	11	75	2	12	76
" 10	52	Kazimota	25	M.	1st	5,100,000	8,120	51	31	15	4	86
Sept. 29	53	Aliabu	25	M.	1st	5,400,000	11,600	28	60	10	2	88
" 18	54	Sururu	20	M.	3rd	4,900,000	3,800	60	22	12	6	66
" 24	55	Omera	14	M.	Early stage	5,300,000	9,100	32	50	9	9	85
" 27	56	Sebugao	20	M.	3rd	5,000,000	9,070	39	45	13	3	92
Oct. 19	"	"	"	"	"	5,200,000	7,500	29	60	7	4	94
" 17	57	Kasussi	25	M.	Early stage	4,800,000	8,700	28	58	6	8	94

Following the suggestion of Mr. Plimmer, who found that the trypanosomes were more numerous in the blood of animals at night than in the daytime, some observations were made with the object of determining whether this was the case in men. It will be seen from the following table that some periodicity seems to exist in man also. The percentages which are taken as a rough index of the number of trypanosomes present, in a slide, refer to the number of trypanosomes per polynuclear leucocytes counted:—

Date 1904.	Name.	No.	Parasites in blood, daytime.			Parasites in blood, night time.		
			Filar.	Mal.	Tryp.	Filar.	Mal.	Tryp.
					per cent.			per cent.
June 21	Kitsame	... 303	+ 4	+ 8
" 23	"	+ 3	+ 10
" 22	Arcadi	... 69/K.P.	+ 1	+ 1
" "	Asumani	... 69/Z.D.	—	+
" 23	Tenwa	... 302	—	+
" 22	Juma	... 69/J.Q.	—	—
" "	Hamesi	... 69/F.V.	+ 1	+ 2
" "	Juma	... 69/J.Q.	—	—

5. *The cells of the cerebro-spinal fluid of sleeping sickness cases taken during life by lumbar puncture are lymphocytes and are more numerous in the late stages of the disease.*

Having seen that the lymphocytes of the blood are increased in number, the next step to take was to determine whether during life these elements were present in number in the cerebro-spinal fluid of sleeping sickness cases. The total number of cells per e.mm. of cerebro-spinal fluid was determined by means of a Thoma-Zeiss apparatus. Stained preparations were also made of the sediment obtained by centrifuging. The cells were found to be all lymphocytes.

From a study of the following table it will be seen that there is a progressive rise in the number of lymphocytes in the cerebro-spinal fluid as the disease advances, the following are the averages:—

23 per e.mm.	Early Stage (Polyadenitis)
257 per e.mm.	1st Stage (S.S.)
355 per e.mm.	2nd Stage (S.S.)
730 per e.mm.	3rd (S.S.)

This result is of considerable interest when considered in connection with the post-mortem appearances found in the nervous system of sleeping sickness cases; these were shown by

Mott to consist essentially of an accumulation of mononuclear cells in the lymph spaces of the brain.

The following table shows the result of the estimation of the specific gravity of, the reaction of, the total and differential enumeration of the cells and the presence or absence of trypanosomes in, the cerebro-spinal fluid taken during life by lumbar puncture from cases of sleeping sickness at all stages of the disease :—

Date, 1904.	No.	Name.	Age.	Sex.	Stage of Disease.	Specific Gravity.	Reaction.	Total Cells, per c.mm.	Percentages.				Tryps. in C. S. F.
									P. N.	S. M.	L. M.	E.	
May 4	1	Kaboe Jongira	14	M.	1st	1,008	Alk.	400	Present.
" 9	2	Sumani	18	"	2nd	1,008	"	300	2	75	23	...	"
" 10	3	Arisati	7	F.	1st	1,007	"	300	1	77	22	...	"
" 11	4	Mundu	38	M.	2nd	1,008	"	300	...	85	15	...	"
" 14	5	Juma	25	"	1st	...	"	300	2	74	25	...	"
" 17	6	Arkadi	25	"	2nd	1,008	"	1,090	2	78	20	...	"
" 18	7	Simoni	20	"	2nd	1,008	"	156	.5	80	20	...	"
" 20	8	Nuwa Kikabanga	31	"	2nd	...	"	680	.5	75	25	...	"
" 20	9	Josua	20	"	Early	...	"	30	Absent.
" 21	10	Lotone	40	"	3rd	...	"	78	...	85	15	...	Present.
" 23	11	Zakayo	15	"	2nd	...	"	280	...	All mononuclears.			"
" 25	12	Asmani	14	"	3rd	...	"	670	...	"	"	...	"
" 26	13	Abraham	18	"	3rd	...	"	2,340	...	"	"	...	"
" 29	14	Zake	25	"	Early	...	"	16	...	"	"	...	"
" June 3	15	Bafrawala	18	"	2nd	...	"	578	...	"	"	...	Absent.
" 5	16	Sempagana	10	"	2nd	...	"	375	...	"	"	...	Present.
" 6	17	Sabakaki	12	"	3rd	...	"	94	...	"	"	...	"
" 7	18	Jordien Murjan	35	"	1st	...	"	30	...	"	"	...	"
" 7	19	Tenwa	25	"	Early	...	"	16	...	"	"	...	Absent.
" 7	20	Kitsami	26	"	"	...	"	30	...	"	"	...	"
" 10	21	Msubika	17	F.	2nd	...	"	280	...	"	"	...	Present.
" 6	22	Suedi	35	M.	2nd	...	"	730	...	"	"	...	"
" 15	23	Arcadi	25	"	3rd	...	"	970	...	"	"	...	"
Aug. 18	24	Zururu Mzee	25	"	3rd	...	"	219	...	"	"	...	"

6. *The gland juice in a certain proportion of cases in the last stage of the disease becomes infected by bacteria, especially diplo-streptococci.*

In view of the fact that some importance has been attached to streptococci as playing a part in the causation of sleeping sickness, a series of examinations of the gland juice were made in a number of cases at intervals in the course of the disease microscopically and culturally. The result of these observations showed, that a number remained cases of pure trypanosoma infection to the end, the cultures made from the glands, blood and cerebro-spinal fluid remained sterile. On the other hand in a proportion of cases an invasion, chiefly by diplo-streptococcus, did occur, but by the results of the examination at different stages of the disease it was possible to locate it to the final stage of the disease, when the patient was practically moribund.

These cases at this stage of the disease have invariably numerous foci of suppuration on the hands and feet due to jiggers, also there is frequently before death a purulent discharge from the gums: their vitality and resisting power is a negative quantity.

The results are fully recorded in the histories of the cases of sleeping sickness given in the Appendix. The following table shows the frequency of the occurrence of this bacterial invasion in sleeping sickness cases and the period of the disease at which it takes place:—

No.	Name.	Age.	Sex.	Date of Death. 1904.	Date of Examinations. 1904.	Diplo-streptococci in :—			Cerebro-spinal Fluid.
						Lymph glands.	Blood.		
1	Sabakaki	8	M.	June 18	March 15 June 6 " 18	Absent " " Absent Absent. Absent.
2	Zeridan	16	"	March 24	March 17 " 24	" Present	... Present	... Present.	... Present.
3	Abimerika	22	"	June 11	March 19 April 21 June 4 " 11	Absent " " " Absent Absent. Absent.
4	Wasiwa	18	"	July 22	March 25 June 30 July 22	" " " Absent Absent. Absent.
5	Kirongo	40	"	June 16	March 28 June 12	" Present (Pneumococcus) B. Coli Com. Pneumococcus. Pneumococcus.
6	Zumageza	18	"	May 8	April 9 " 20 May 8	Absent " Present
7	Usmani	20	"	" 19	April 25 May 9 " 19	Absent " " Absent Absent Absent.

No.	Name.	Age.	Sex.	Date of Death. 1904.	Date of Examinations. 1904.	Diplo-streptococci in :—		
						Lymph glands.	Blood.	Cerebro-spinal Fluid.
8	Msake	16	M.	May 24	May 6 " 24	Absent "	... Absent	... Absent.
9	Hamisi	12	"	July 24	May 5 July 12 " 24	" " Present Present Present.
10	Arcadi ...	25	"	July 27	May 17 June 1 July 14 " 19 " 21 " 27	Absent " Present " " " Present Present
11	Sempagama	8	"	June 15	March 14 June 5 " 15	Absent " " Absent Absent.
12	Usmani	14	"	26	May 25 June 19 " 25 " 26	" " Present " Present " Present.

7. *Does the injection of a pure culture of diplo-streptococci obtained from sleeping sickness cases modify the course of the disease produced in monkeys by the Trypanosoma gambiense?*

Dr. Mott in a letter forwarded to the Commission suggested that it would be of interest to test the effect of injection of diplococci obtained from cases of sleeping sickness into monkeys suffering from trypanosoma infection. A pure culture in broth of a diploeoccus obtained from the cerebro-spinal fluid of a case of sleeping sickness was used for the experiments. The injections were made subcutaneously and a large number of germs were introduced. The effects of the injection were observed in a healthy monkey, a monkey infected with *Trypanosoma gambiense*, which showed at the time of injection the parasite in the blood and only slight clinical manifestations, and finally a monkey infected with the same trypanosoma, but showing very well marked clinical signs. This injection did not produce any alteration of temperature or other morbid sign in the healthy animal, nor in the animal infected by the trypanosomes, but at an early stage of the disease; in the monkey which was seriously ill at the time of injection it produced a local suppuration. It is apparent from these observations that the streptococcus found in the tissues of sleeping sickness cases has very low pathogenic properties, and only gains a footing at all when the resisting power of the tissue is greatly diminished. It does not modify the course of the disease produced in monkeys by the *Trypanosoma gambiense*.

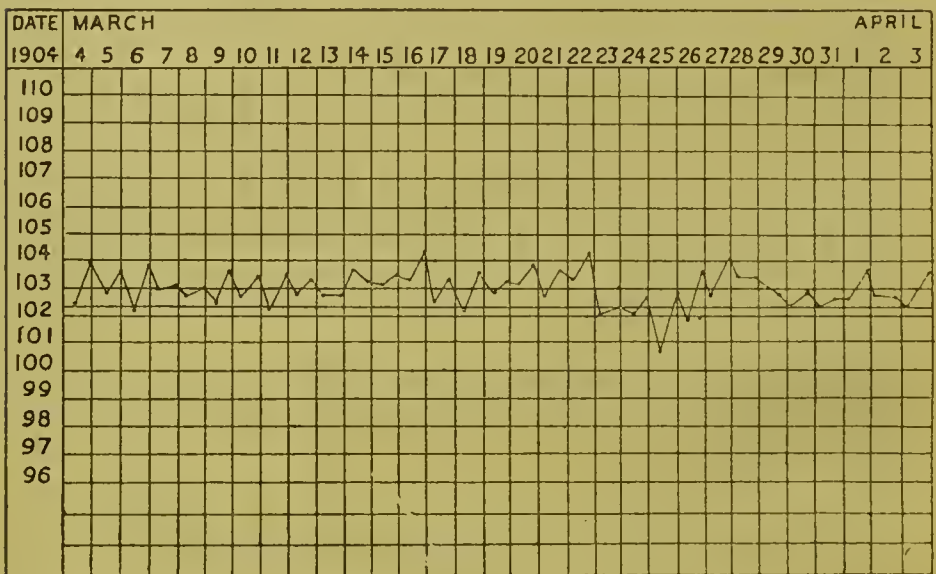
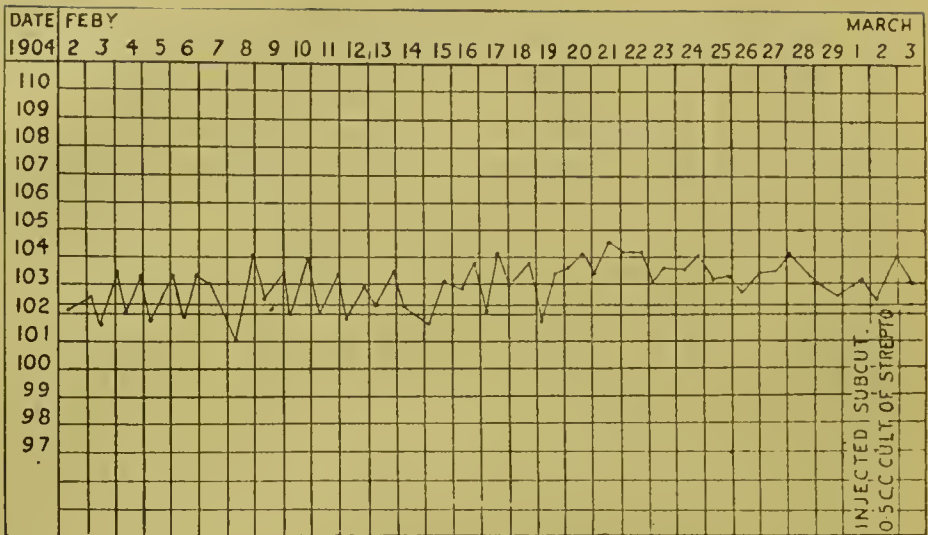
The following experiments show the effect on monkeys of the injection of a pure culture of diplo-streptococci from sleeping sickness cases:—

EXPERIMENT 285. MONKEY, SMALL (*Cercopithecus sp.*).

To note the effect of subcutaneous injection of a pure culture of diplo-streptococcus obtained from the cerebro-spinal fluid of a case of sleeping sickness.

March 2, 1904. Injected subcutaneously into left thigh 0.5 c.c. of a broth culture of diplo-streptococcus from the cerebro-spinal fluid (post-mortem) of case 69 K.K. The growth was 48 hours old. The growth was abundant. It was proved pure by microscopic examination and by sub-culture on agar. March 9. No local reaction at the seat of inoculation. The general health, temperature, etc., of the animal is normal.

The following chart shows the temperature curve before and for some time after the inoculation:—



... The temperature has since been regularly taken. It remains quite normal and the general condition of the animal is good.

Remarks.—This experiment shows that when a pure culture of the diplo-streptococcus is injected subcutaneously in considerable quantity into a healthy monkey it produces neither local nor general reaction. The pathogenic power must be low. It is incapable of producing any of the signs of sleeping sickness commonly met with in the infection produced by the *Trypanosoma gambiense* in monkeys.

EXPERIMENT 8. MONKEY (*Cercopithecus* sp.).

To note the effect of subcutaneous injection of blood from case of trypanosoma fever into a monkey and secondly, the subcutaneous injection of a pure culture of streptococcus obtained from a case of sleeping sickness.

April 3, 1903. Injected subcutaneously a small quantity of blood from case J.M., whose blood is seen to contain trypanosomes this morning. The blood taken only amounted to a drop or so and had firmly clotted.

April 4. Injected about 1 c.c. of blood from same case.

May 11. Injected 2 c.c. of blood from Jordien Murjan.

August 25. No symptoms of sleeping sickness.

January 26, 1904. The animal has begun to look seedy. His expression is rather dull and his coat is not in good order.

March 28. Injected subcutaneously into right interscapular region 1.0 c.c. of a broth culture 72 hours old from Case 69 Q.Q. first remove. It was proved to be a pure culture of diplo-streptococcus by cultivation on agar and microscopic examination.

April 15. The general condition of the animal since the injection of the culture of streptococcus has remained unchanged.

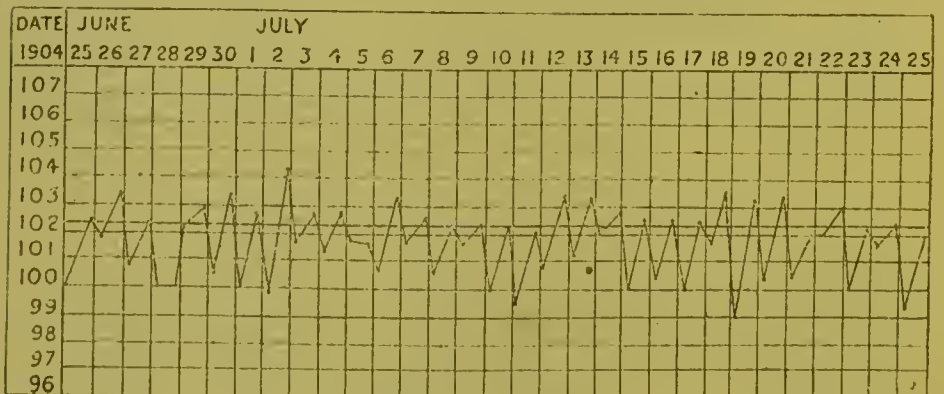
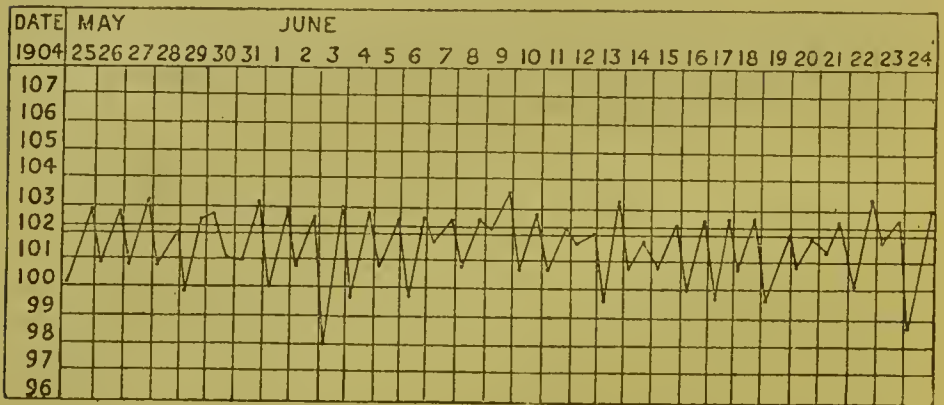
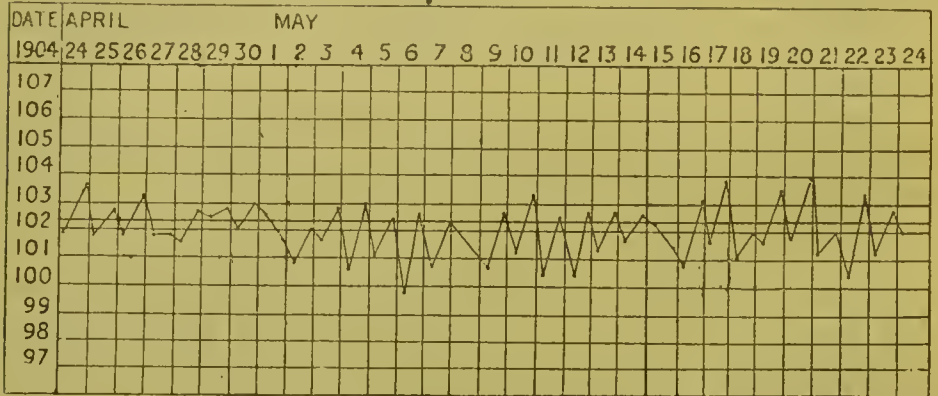
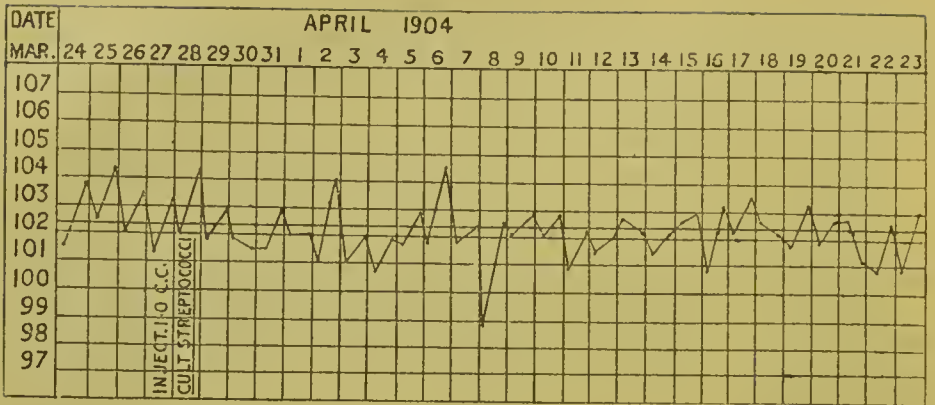
August 22. The animal is now distinctly ill. His coat is out of condition, and he is much thinner. He sits crouched up a good deal.

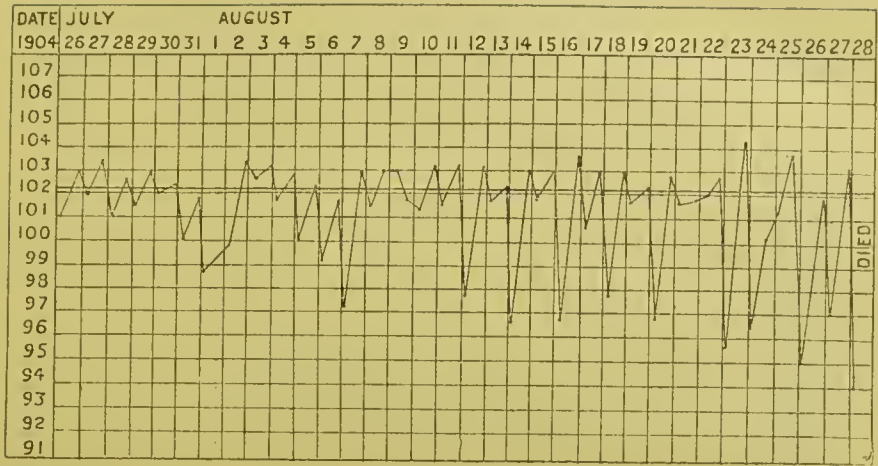
August 23. He has now a very dull drowsy expression and his head is constantly drooping between his knees.

August 27. He is now very weak and is lying on his side. The trypanosomes were very numerous in his blood; lumbar puncture was performed. The cerebro-spinal fluid contained some red cells. Active trypanosomes were present.

August 28. The animal is dying. Lumbar puncture performed; cerebro-spinal fluid clear. On microscopic examination active trypanosomes present and a few red cells.

The following chart shows the course of the disease after the injection of the streptococcus:—





The following table shows the presence or absence of trypanosomes and streptococcus in the blood :—

Date.	Parasites in the blood.			Parasites in C.S.F.	
	Fil.	Mal.	Tryp.	Strept.	Tryp.
1903.					
April 9	—	—
" 11	—	—
" 23	—	—
" 30	—	—
May 7	—	—
" 14	—	—
" 21	—	+
" 28	—	+
June 4	—	+
" 11	—	—
" 18	—	+
" 25	—	+
July 1	—	+
" 23	—	+
" 31	—	—
Aug. 7	—	—
" 13	—	+
" 20	—	+
" 28	—	+
Sept. 4	—	+
" 12	—	+
" 25	—	—
Oct. 8	—	—
Nov. 5	—	—

The following table shows the presence or absence of trypanosomes in the blood and cerebro-spinal fluid from June 9th :—

Date 1904.	Parasites in the blood.			Parasites in C.S.F.	
	Filar.	Malar.	Tryp.	Strepto.	Tryp.
June 9	...	—	+
" 16	...	—	+
" 24	...	—	+
July 2	...	+	+
" 15	...	+	+
" 22	...	+	+
" 30	...	+	+
Aug. 12	...	+	+
" 19	...	—	+
" 26	+
" 27	+	...	+
" 28	+	—	+

August 28, 1904. Animal killed by chloroform. Post-mortem at once.

The body is distinctly emaciated. The coat is very much out of condition. No sores. Pupils equal and normal. Slight general enlargement of lymphatic glands. Some increase of fluid in pericardial cavity, none in pleural or peritoneal.

Brain.—On removing the calvarium and reflecting the dura mater, there is seen to be some injection of superficial vessels, and slight flattening of the convolutions, otherwise nothing noteworthy. A culture in broth was made from the cerebrospinal fluid—this remained sterile.

Spinal cord.—There is some hæmorrhage into the theca from the puncture, otherwise it is normal. Brain removed entire with spinal cord roots, ganglion, and nerves for future investigation.

Heart.—Nothing noteworthy. The blood of this organ contains many trypanosomes not modified in shape. A culture in broth was made from the blood, which remained sterile.

Lungs.—Both show minute areas of embolism studded through the substance. On microscopic examination these are seen to contain altered trypanosomes.

Peritoneal cavity.—On opening the cavity a number of "bladder-like" structures of various sizes containing fluid are seen in the folds of the peritoneum bulging into the cavity. To find out the exact relation of parts the whole abdominal contents were turned out and floated in water. After dissection it was determined that the "bladders," which were quite transparent, except for an opaque spot at one point and contained a clear fluid, lay between the layers of the omentum, and on cutting these through they became free. It was also seen that these "bladders" were embedded in the substance of the liver and bulged out of its substance on its various surfaces and became adherent to the surrounding structures. The fluid in the cysts was quite clear, some of it was centrifuged and examined under the microscope, but no hooklets or similar structures were seen.

Liver.—Removed entire for the further study of the cysts contained.

Spleen.—Slightly enlarged. Slight general enlargement of superficial area. No points of suppuration on section.

Remarks.—This is an interesting experiment because (1) It demonstrates the long course which the trypanosoma infection, as in man, may run (from inoculation until the death of the animal, nearly 18 months), and that only towards the close of life were the characteristic signs of the disease present. Both in men and in monkeys the malady may either run an acute, or, as in this case, a very chronic course. The disease in monkeys, therefore, has a strictly parallel course to that observed in man. (2) During the course of the trypanosome infection, when the temperature became somewhat irregular, but otherwise no marked signs were manifest, an injection of a pure culture of diplo-streptococcus rich in germs was made to determine the effect. The injection was followed by no effect, so far as could be observed, either locally or generally, and the animal sickened and died many months afterwards with a trypanosome infection. It is possible that the general condition of the animal was lowered by the state of the liver, which permitted the trypanosomes to get the upper hand.

EXPERIMENT 99. MONKEY (*Cercopithecus* sp.).

To observe the effect of infection of the monkey by tsetse flies which had fed on a sleeping sickness patient 24 hours previously, and the effect of subcutaneous injection of a pure culture of diplo-streptococcus on the course of this infection.

July 23, 1903. Trypanosomes were noted in the blood for the first time; the feeding was begun on May 15, 1903.

January 15, 1904. Animal out of condition generally, but is still fairly active.

February 14. Animal is very weak and thin. He is crouched up and frequently his attitude is very characteristic, the head drooping between his knees.

February 22. Animal lies about a good deal. He takes his food better. His temperature is still swinging.

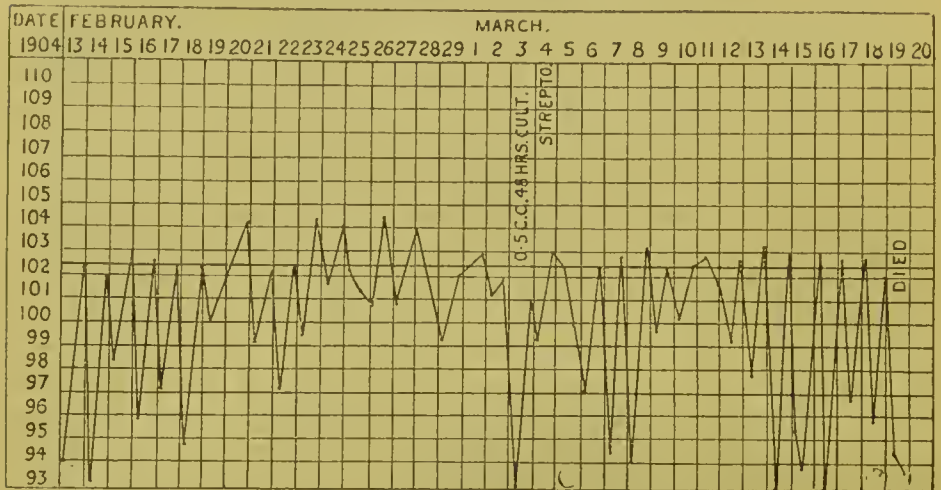
March 2. Injected under the skin of left thigh 0.5 c.c. culture in broth of a diplo-streptococcus obtained from the cerebro-spinal fluid of a case of sleeping sickness taken post-mortem. The growth was 48 hours old. It was proved to be a pure culture of diplococci by microscopic examination and by culture in agar. The growth was abundant and grew in the form of balls with clear fluid between.

March 13. The animal, as formerly, is in the usual characteristic attitude. The saliva tends to dribble from his mouth. The glands in his left groin are distinctly enlarged.

March 19. Animal is in a moribund condition, passing its motions under it and unable to rise. Saliva is dribbling from its mouth, a gland in right groin was distinctly enlarged; this

was removed and found to contain pus. Smears showed under the microscope diplococci and "bodies" stained blue which appeared to be degenerated trypanosomes.

The following chart shows the temperature curve:—



The following table shows the presence or absence of trypanosomes and streptococci in the lymph glands, blood and cerebro-spinal fluid:—

Date.	Parasites in glands		Parasites in blood.			Parasites in C.S.F.	
	Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.
1903.							
July 23	—	+	+
Aug. 3	+	+
" 21	+	+
Sept. 25	+	+
Oct. 8	—	+
Dec. 10	—	—
" 18	+	—
Jan. 15	+	+
" 28	+	+
Feb. 8	+	+
" 21	+	+
" 29	+	+
Mar. 6	+	+
" 13	+	+
" 19 ...	+	+	...	+	+	+	—

March 20. Animal died in the night. Post-mortem 9 a.m.

The body is markedly emaciated. Lymphatic glands in both femoral regions are enlarged—glands in right femoral region are suppurating. Glands in axilla and neck are enlarged, but not suppurating. Pupils equal and normal. No increase of

fluid in pleural or peritoneal cavities, slight increase in pericardial.

Brain.—On removing the calvarium the dura mater is seen to be normal; on reflecting it, the convolutions are seen to be slightly flattened and the superficial vessels are injected; the sub-arachnoid fluid is increased—no active trypanosomes were seen microscopically, but the animal had been dead for some time. A pure culture of a streptococcus was obtained from the cerebro-spinal fluid.

Heart.—Nothing noteworthy. Blood from this organ examined microscopically showed many trypanosomes. Malaria is also present.

Lungs.—Are both healthy.

Liver, Spleen, and Kidneys.—Show nothing noteworthy.

Intestines.—Are healthy.

Lymph Glands.—In omentum and mesentery distinctly enlarged.

Remarks.—This experiment demonstrates several points of importance. The first being that it is possible to convey the trypanosoma of sleeping sickness from man to monkey after an interval of 24 hours. Secondly, that the disease produced in the monkey by the fly infection presents the same characters as that produced by inoculation of cerebro-spinal fluid or blood from a case of sleeping sickness. This animal presented towards the close of its life a typical picture of a sleeping sickness case.

This experiment is, finally, of interest and importance from the fact that 15 days before its death it had been injected with a pure culture of diplococci obtained from a case of sleeping sickness. So far as we could observe, the course of the disease was uninfluenced by the injection, the only noteworthy feature being a slight suppuration in one of the groups of lymphatic glands near the site of inoculation. Portions of the nervous system and glands have been preserved for minute investigation and the results of the examination will be of interest.

8. *Has the so-called Trypanosoma Fever any connection with Sleeping Sickness?*

Since the publication of the last Report the observations on the five men in whose blood the trypanosomes were first discovered in March, 1903, have been continued.

Two of these, Karala Barigi and Bara Risgallah, died of pneumonia in April and May, 1904, respectively; of the others, Jordien Murjan appears to be undoubtedly in an early stage of sleeping sickness. He has gradually developed the characteristic signs of the malady. Trypanosomes are now always found in his cerebro-spinal fluid. Tabula presents some of the features of the disease, but is still able to do his work and has not yet shown trypanosomes in the cerebro-spinal fluid.* Kumsarsabba is in a similar condition.

* Lieut. Gray writes, February, 1905, "That Tabula now shows trypanosomes in the cerebro-spinal fluid, and distinct signs of sleeping sickness."

In addition to the above, in order to extend the observations on this most important stage of the disease, five natives were picked out, from a batch of prisoners from Usoga, having enlarged glands in the neck. On examination trypanosomes were found in the lymph juice of each. These men are being kept in hospital and their condition is being carefully observed. We have also observed the action of arsenic on the *Trypanosoma gambiense* in these men. None of them show any of the characteristic features of sleeping sickness, and the trypanosomes are not present in the cerebro-spinal fluid. In fact, with the exception of enlargement of the lymphatic glands and slight fever the general condition of the men is good.

The importance of this stage of the disease is so great that a full account of the observations on these five natives is given. The diet has been increased, in addition to bananas, a ration of meat is given twice weekly. It will be seen from the tables that since admission the trypanosomes are less frequently found in the lymphatic glands and blood. Up to date they have improved remarkably in general condition and have rapidly put on flesh. The after history of these cases, maintained under the above conditions, will be of considerable interest.

EXPERIMENT 31. KARALA BARIGI. MALE.

District, Singo. Occupation, policeman. Tribe, Mundu, Nubian.

April 24, 1903. Patient states that he has been six months in Entebbe. His illness began on March 10. He asserts that at present he feels quite well and has no headache or other symptoms. There are no enlarged glands in the neck, but in the axillæ they are as large as peas and they are also enlarged in the groin. His tongue is moist and furred. His speech is fluent. Pulse 120, fair. His heart sounds are normal.

September 23, 1903. There is slight general enlargement of the lymphatic glands. Slight tremor of hands and tongue.

February 6, 1904. Glands distinctly enlarged in the left post triangle of neck. Cerebro-spinal fluid flowed out very freely, a few flakes in it.

April 4. There is slight œdema of right leg, which he states has been present for about a month. Tremors of hands present. Glands distinctly enlarged in both posterior triangles. A gland was excised from the right posterior triangle. A drop of the juice of this gland examined under the microscope showed many active trypanosomes. Stained preparation showed well-formed trypanosomes and also many apparently modified trypanosomes. Gland was preserved for further examination.

April 16. There is œdema of both feet and legs. He was admitted into the native hospital to-day for double pneumonia.

The temperature remained practically normal up to the onset of the pneumonia.

The following table shows the presence or absence of trypanosomes in the lymphatic glands, blood, and cerebro-spinal fluid:—

April 18. Patient died this morning. It is much to be regretted that no post-mortem examination could be made on this very important case.

CASE 61. JORDIEN MURJAN. MALE. AGE 36.

District, Muru. Nubian. Prisoner for last three years.

March 31, 1903. Admitted to hospital. He is an old Soudanese mutineer and lives as a prisoner in the jail.

No fellow prisoners have had sleeping sickness. He has no oedema, and no noticeable swelling of glands. His tongue is healthy, but shaky. There is no tremor of the hands. His speech is normal and pulse 144.

August 18. This patient at the present date has not any marked symptoms of sleeping sickness. At the same time there is slight general enlargement of lymphatic glands, his expression is dull, there is some tendency to tremor of the tongue and fingers and his pulse is rapid.

September 21. Expression is dull and heavy. Complains of no pains. Appetite good. Pulse 136. Slight tremors of tongue and fingers.

November 9. No definite signs of sleeping sickness. Pulse 120. Fine tremors of tongue.

December 26. Tremors of fingers distinct. Trypanosomes present in cerebro-spinal fluid.

February 1, 1904. General condition as before.

March 21. A gland in left anterior triangle of neck was removed; active trypanosomes were present in the juice.

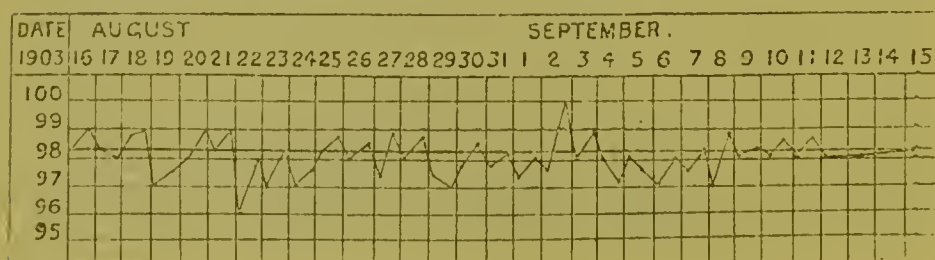
June 7. Pulse 104. No pain. Tremors of hands and tongue present. Oedematous swelling of both legs. Cerebro-spinal fluid contains active trypanosomes—no red cells. He is reported to be "very dull and stupid and fit for very little work."

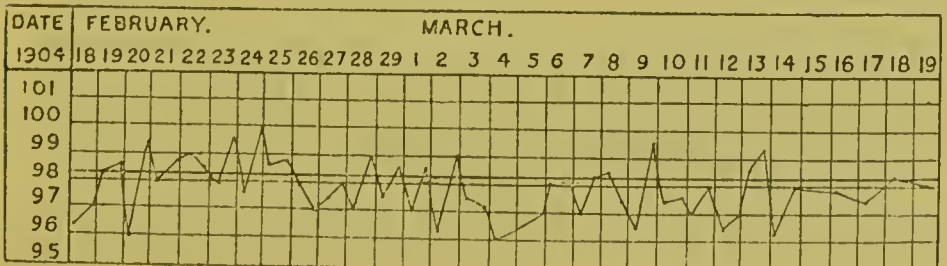
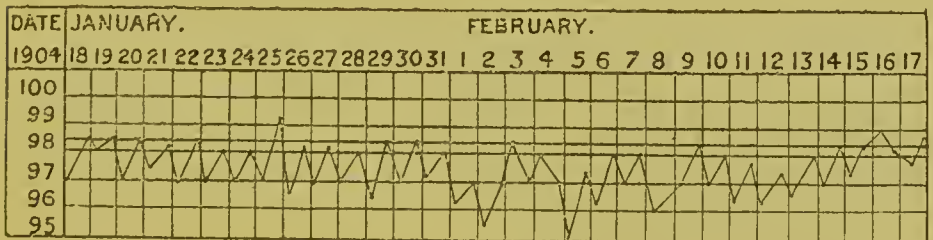
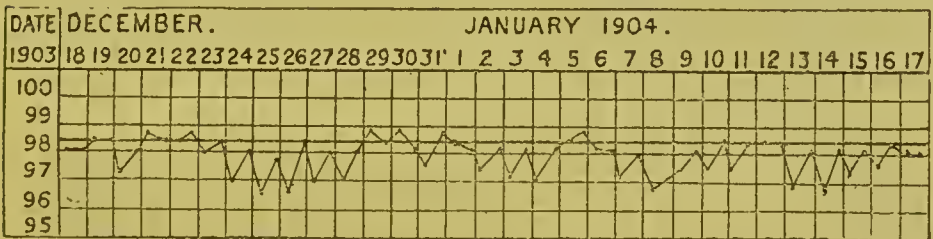
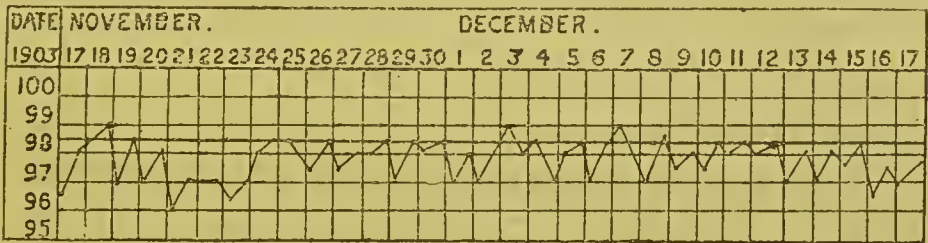
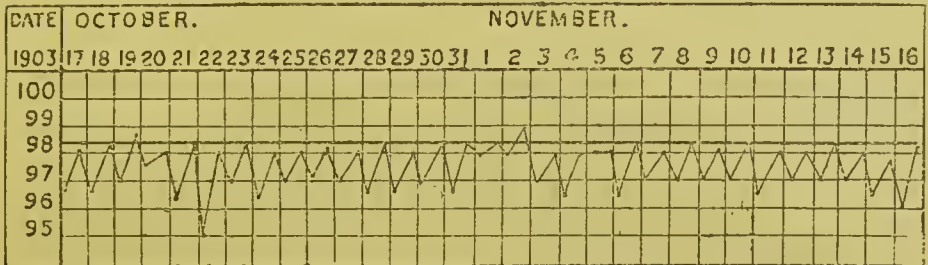
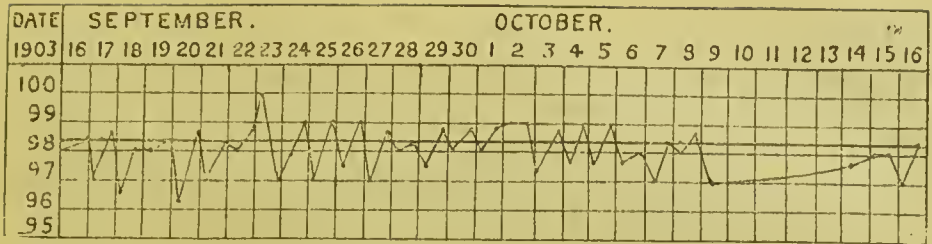
July 18. Complains of pain in head, arms and chest, also of itching. Pulse 125. Active trypanosomes in cerebro-spinal fluid; no red cells in deposit.

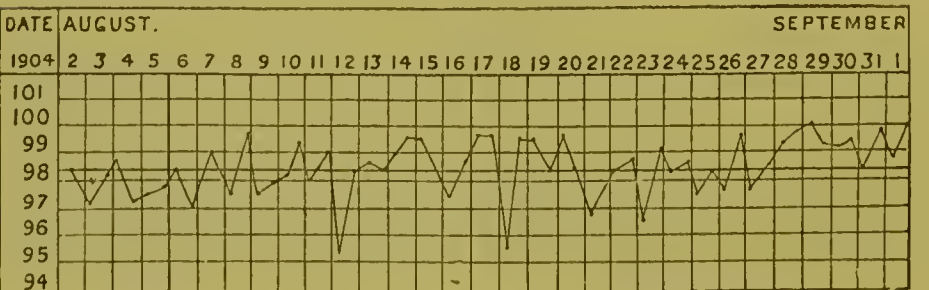
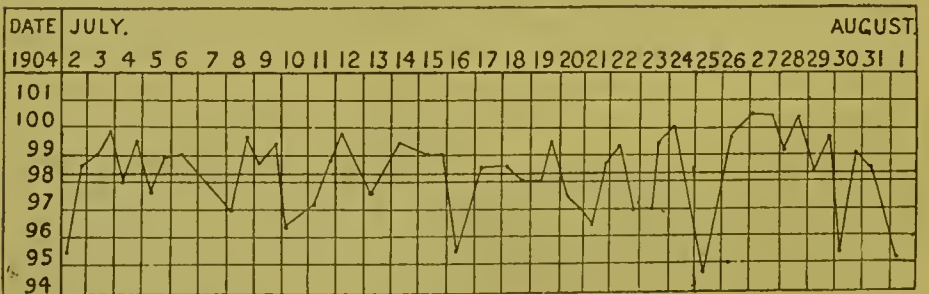
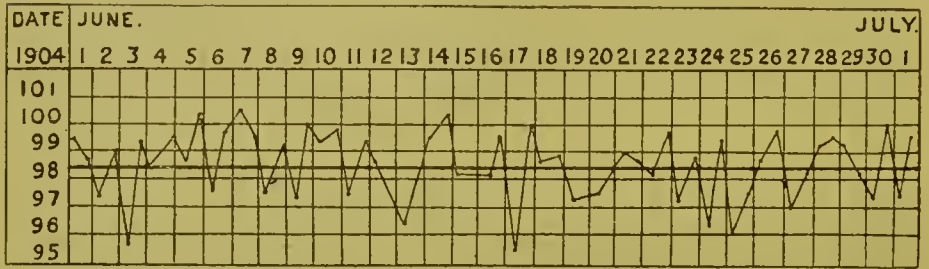
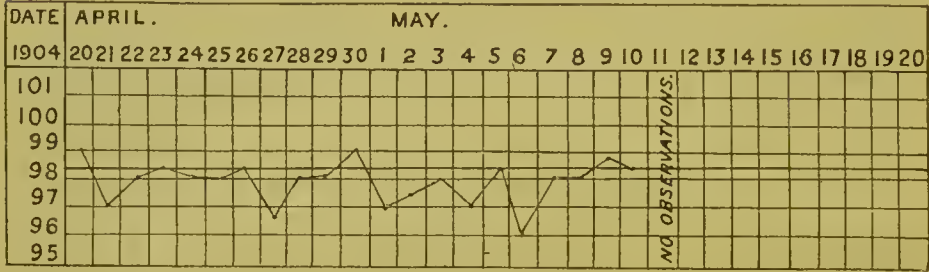
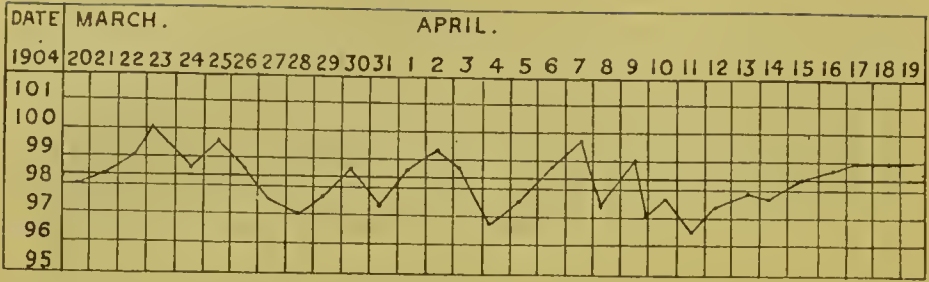
August 25. Complains of no pain. Pulse is 120. Oedema of right foot. Trypanosomes present in cerebro-spinal fluid; no red cells.

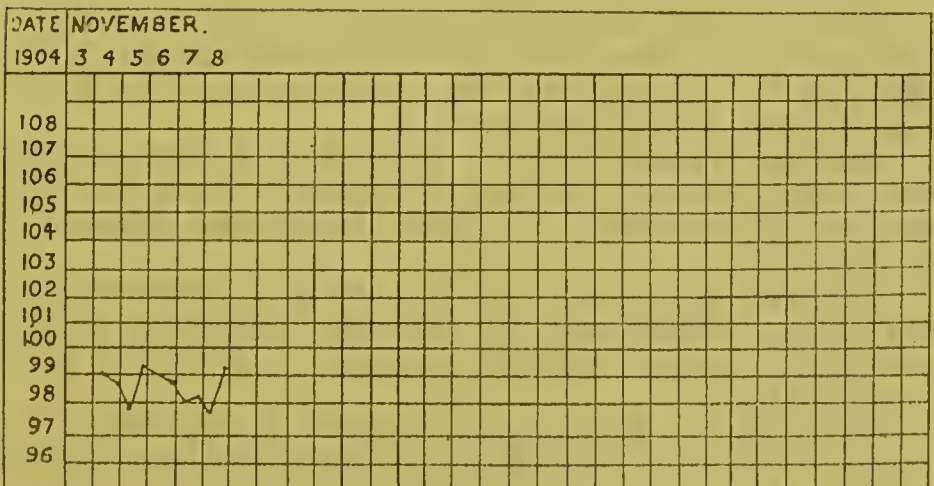
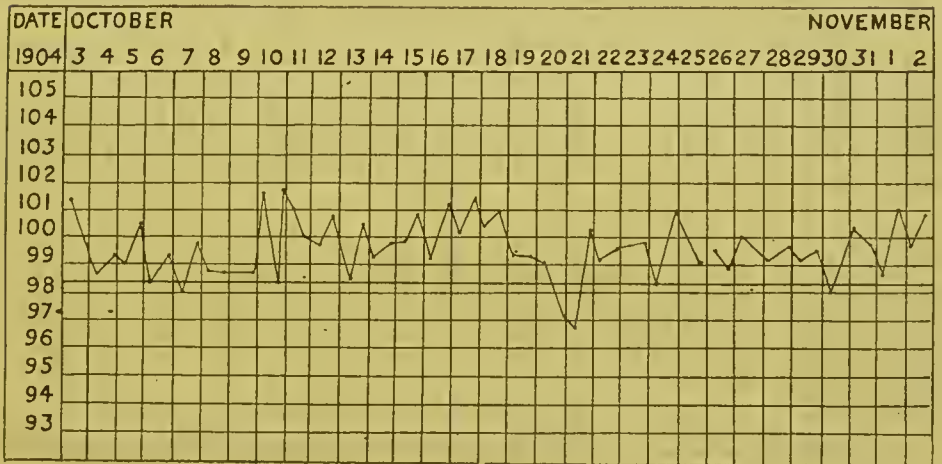
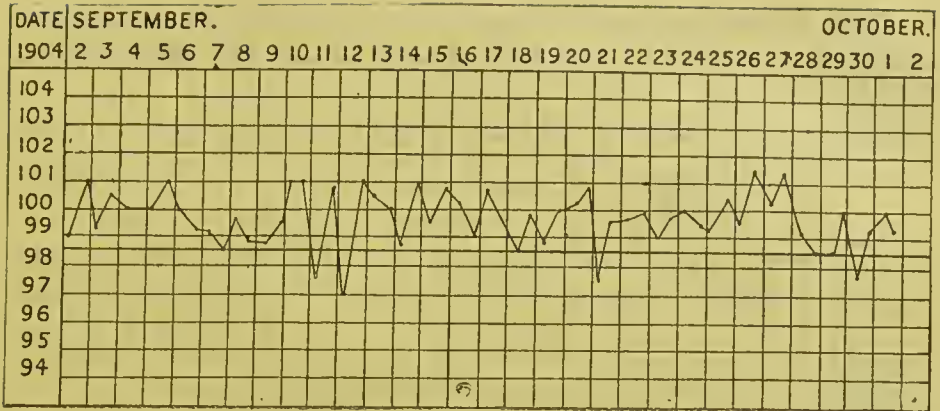
October 2. Tremors of hand. No pain. Slight oedematous swelling of left foot. Trypanosomes in cerebro-spinal fluid; no red cells in deposit.

The following chart shows the course of the disease:—









The following table shows the presence or absence of trypanosomes in the lymphatic glands, blood and cerebro-spinal fluid:—

Date.	Parasites in Glands.		Parasites in the Blood.			Parasites in C.S.F.	
	Strepto.	Tryp.	Filar.	Malar.	Tryp.	Strepto.	Tryp.
1903.							
March 31	+	...	—
April 1	+
" 2	+
" 3	+
" 17	—
May 1	—	...	+	...	—
" 11	+	...	—
" 25	+	...	—
June 9	+	...	—
" 23	+	...	—
July 22	+	...	+
Aug. 18	+
Sept. 21	—	...	+	...	—
Nov. 9	—	...	+	...	—
Dec. 26	—	...	+	...	+
1904.							
Feb. 1	—	...	+	...	—
March 21	—	...	+	...	—
June 7	...	+	—	...	+	...	+
July 18	...	+	—	...	+
Aug. 25	...	+	+	...	+
Oct. 2	...	+	+	...	+

EXPERIMENT 68. BARA RISGALLAH (MALE). AGE 35 YEARS.

Trypanosoma fever. Tribe Lendu. Occupation police. Lives in hut in police lines.

April 21, 1903. Admitted to hospital. This man states he had been ill ten days, and that the ailment began with a shivering fit. He also says he had a sickness like this in Kampala four or five years ago.

April 24. Patient looks ill. There is no oedema and only the glands in the groin are slightly enlarged. His pulse is 108, feeble and compressible. The heart sounds are normal. He has no tremors.

November 10. Patient fell asleep while on duty during the day. Some enlargement of lymphatic glands in anterior triangles of neck. Distinctly enlarged in axilla and groin. Pulse 160 weak.

December 19. Patient was in hospital for synovitis of left knee and oedema of both legs. He has been lying about a good deal lately. Pulse 96 feeble.

February 8, 1904. Patient looks dull and heavy. Pulse 108.

March 30. Glands enlarged in both triangles of neck. Pulse 100. Rather emotional—fits of weeping. Tremors of hands. Gland excised from right anterior triangle contained active trypanosomes. No streptococci seen in the films of the juice.

April 27. Admitted to hospital complaining of cough and fever. There was slight oedema of both legs near ankles. Slight impairment of note at right apex. Breathing rapid. Sputum is watery.

May 1. Percussion of chest shows dullness both anteriorly and posteriorly on the right side more marked at upper part of chest. Vocal fremitus is increased. Breath sounds are bronchial in character and are accompanied by crepitations. Sputum is sticky—has a rather greenish colour.

May 4. Dullness is marked all over chest on right side anteriorly and posteriorly. Liver extends four inches below costal margin. Some jaundice of conjunctivæ.

The temperature remained normal up to the onset of the pneumonia:—

The following table shows the result of enumeration of the blood corpuscles, the presence or absence of trypanosomes in glands, blood and cerebro-spinal fluid:—

Date.	R.B.C.	W.B.C.	S.M.	L.M.	P.	E.	Hb. Per cent.	Parasites in glands.		Parasites in blood.			Par. in C.S.F.	
								Filar.	Tryp.	Filar.	Mal.	Tryp.	Tryp.	Strepto.
1903.														
April 21	-	...	+	...	+	-	...
May 4	+	-	...
" 11	-	...	+
" 26	+	...	+	-	...
June 24	+	...	+	-	...
July 24	+	...	+	-	...
October 24	-	...	+
November 10...	-	...	+	-	...
December 19	+	...	+	-	...
1904.														
February 8	+	...	+	-	...
March 30	...	6,870	29	11	59	1	+	-	...	-
April 26	23	8	69	0
" 27	4,500,000	6,200	14	8	78
" 29	3,800,000	17,800	10	11	79	...	66
" 29	3,600,000	15,000	6	7	87	...	66
" 30	3,900,000	16,200	22	6	72	...	70
May 2...	3,500,000	15,500	13	4	83	...	68
" 3...	3,800,000	27,100	7	7	86	...	75
" 4...	4,000,000	26,500	6	4	90	...	80

May 5, 1904. Patient died at 5 a.m. Post-mortem one hour after death.

The body is that of a well built and fairly well nourished man. General enlargement of superficial lymphatic glands. Pupils normal and equal.

On opening the body a considerable quantity of straw coloured fluid escaped from the right pleural cavity, no increase of pericardial or peritoneal.

Brain.—On removing the calvarium the dura mater is found to be normal. On reflecting that membrane the sulci of the convolutions of the brain were seen to be filled up with jelly-like exudation. The superficial vessels showed some injection and the convolutions were somewhat flattened. Towards the base of the brain over the medulla, pons and cerebellum there was a considerable amount of exudation of a thicker nature. The general appearance of the brain somewhat resembled that met with in cases of sleeping sickness. Cerebro-spinal fluid was increased; 5 c.c. were centrifuged, but no active trypanosomes were found. A cocco-bacillus was present. Portions of the brain were preserved for further examination.

Heart.—Muscle is pale and flabby, otherwise healthy.

Lungs.—Right, there is some recent lymph on surface, the whole lung being in a state of pneumonic consolidation. The upper lobe being in a state of grey hepatisation, the lower showing a condition of red hepatisation. Left is healthy.

Liver.—Is markedly enlarged, extends four inches below costal margin. On section, is pale and bile stained.

Spleen.—Distinctly enlarged, capsule is thickened, firm on section.

Kidneys.—Nothing noteworthy, intestines normal.

Glands.—Deep cervical are distinctly enlarged. Smears of the glands showed no streptococci, no fully formed trypanosomes were seen.

Remarks.—This man originally came under observation as a case of trypanosoma fever. For the past year his blood, glands and cerebro-spinal fluid have been regularly examined. During life he had several of the signs and symptoms met with in sleeping sickness cases, viz., enlargement of the lymphatic glands and oedema, and others indicating early involvement of the nervous system, i.e., rapid pulse, tendency to drowsiness, tremors and alteration of the facial expression.

Post-mortem the brain presented an appearance resembling that met with in sleeping sickness cases. During the attack of pneumonia he did not present any symptoms indicating acute meningeal change. Although trypanosomes were not found in the cerebro-spinal system, they were abundant in the lymph system, as an examination of the glands showed. This man was almost certainly in a fairly early stage of sleeping sickness.

This experiment should be compared with No. 58.

CASE 302. TENWA. MALE. AGE 25.

District. Usoga.

June 7, 1904. Patient was selected from a group of prisoners from Usoga, on account of enlarged glands in the neck. He asserts that he is quite well. Beyond general lymphatic enlargement, there are no signs of sleeping sickness. The lymph from a gland in the left posterior triangle of the neck was examined and found to contain many active trypanosomes.

July 2. Intra-muscular injections of arsenious acid were begun.

October 16. The general condition of the patient has much improved.

The temperature remained about normal. Slight elevation occurred from time to time, and this was associated with the presence of the parasite in the blood.

The following table shows the result of the enumeration of the blood corpuscles, the percentage of hæmoglobin, the amount of arsenious acid administered, the presence or absence of trypanosomes in the lymphatic glands, blood and cerebro-spinal fluid:—

Date 1904.	R.B.C.	W.B.C.	Hb. per cent.	Percentages.				Parasites in glands.		Parasites in blood.			Parasites in C.S.F.		As ₂ O ₃ in mgs.
				P.N.	S.M.	L.M.	Eos.	Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.		
														Tryp.	
June 7	3,700,000	6,000	66	38	46	13	3	-	+	-	-	-
" 21, 10 a.m.	3,800,000	10,600	70	31	45	22	2	-	+	-	-	-
" 22, "	3,900,000	11,200	72	-	+	-	-	-
" 28, 10 p.m.	-	-	-
" 30, "	4,200,000	7,500	74	39	53	2	6	...	+	+	-	-	10
July 2, 10 a.m.	+	+	-	15
" 3	4,100,000	10,000	72	43	46	4	7	...	+	+	-	-	15
" 4, "	+	+	-	-	18
" 5, "	+	+	-	-	20
" 6	30	59	4	7	...	-	-	-	-	20
" 7	-	-	-	-
" 8	33	61	3	3	...	-	-	-	-
" 11	4,000,000	6,850	68	30	64	3	-	-	-	-	20
" 16	-	-	-	-
" 17	4,300,000	6,600	74	14	69	9	8	...	-	-	-	-
" 25	-	-	-	-
" 26	4,300,000	9,700	72	43	37	14	6	...	-	-	-	-
" 28	29	46	10	15
" 31	-	-	-	-
Aug. 3...
" 6...	42	43	5	10	20
" 8...	31	50	3	16

TENWA 302.

Date 1904.	R.B.C.	W B.C.	Hb. per cent.	Percentages.				Parasites in glands.		Parasites in blood.			As ₂ O ₃ in mgs.
				P.N.	S.M.	L.M.	Eos.	Strept.	Tryp.	Fil.	Mal.	Tryp.	Parasites in C.S.F.
Aug. 11...	23	48	14	5	Per cent.	...
" 14...	26	43	8	23	+ 1	...
" 18...	-	...
" 22...	22	54	10	14	-	...
" 25...
" 27...	+
" 28...	-
" 29...	-
" 31...	-
Sept. 3...	+
" 9...	+
" 15...	+
" 24...	+
" 26...	4,800,000	10,000	72	22	50	8	20	+
" 28...	+
" 29...	+
" 30...	+
Oct. 3...	-
" 7...	+
" 10...	-
" 17...	-
" 21...	-
" 28...	+
Nov. 4...	-

CASE 303. KITSAME. MALE. AGE 26.

District. Usoga.

June 7, 1904. This man is also a prisoner, and was selected on account of enlarged glands, otherwise he presents no signs of sleeping sickness. The lymph obtained from a gland in the left posterior triangle of the neck contained many active trypanosomes.

June 21. Intra-muscular injections of arsenious acid were commenced.

The temperature remained about normal. Occasional slight rises were associated with the presence of trypanosomes in the blood.

The following table shows the result of the enumeration of the blood corpuscles, the percentage of hæmoglobin, the amount of arsenious acid administered, the presence or absence of trypanosomes in the lymphatic glands, blood and cerebro-spinal fluid:—

Date 1904.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.		As ₂ O ₃ in mgs.
			P.N.	S.M.	L.M.	Eos.		Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.	
June 7	4,800,000	12,500	47	30	21	2	80	—	—	—	—	—	—	—	...
" 21, 9.30 a.m.	4,500,000	10,900	52	29	12	7	72	—	+	+	+	+	+	+	...
" 22, 9.30 "	4,600,000	10,930	53	33	10	4	74	—	+	+	+	+	+	+	...
" 22, 10.30 p.m.	4,600,000	...	43	47	7	3	74
" 23, 10.30 a.m.	4,700,000	9,000	42	49	8	1	74	—	+	+	+	+	+	+	...
" 23, 4 p.m.	44	42	10	4
" 23, 10 "	41	46	7	6
" 24, 11 a.m.	4,600,000	8,000	42	44	9	1	76	—	+	+	+	+	+	+	...
" 25, 11 "	4,500,000	6,000	46	42	4	8	80
" 25, 4 p.m.	45	40	11	4
" 25, 10 "	39	54	3	4
" 26, 3 "	4,500,000	5,600	33	55	7	5	80
" 27, 10 a.m.	4,600,000	5,600	41	50	5	4	82	...	+	+	+	+	+	+	...
" 27, 4 p.m.	32	56	8	4
" 27, 10 "	35	55	6	4
" 28, 11 a.m.	4,700,000	5,000	33	56	6	5	82	...	+	+	+	+	+	+	...
" 28, 4 p.m.	39	49	5	7
" 28, 11 "	40	50	4	6
" 29, 11 a.m.	4,400,000	5,300	32	54	5	9	80	...	+	+	+	+	+	+	...
" 29, 4 p.m.	41	50	4	5
" 29, 11 "	40	48	5	7
" 30, 2 "	4,300,000	5,000	37	54	4	4	80
" 30, 11 "	34	60	4	2
July 1, 11 a.m.	4,500,000	5,000	44	48	5	3	78	...	—	—	—	—	—	—	...

Date 1904.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.	As_2O_3 in mgs.
			P.N.	S.M.	L.M.	Eos.		Strept.	Tryp.	Fil.	Mal.	Tryp.		
July 1	34	55	+	7	+	-	-
" 2	4,600,000	5,000	39	51	4	6	...	-	- 22
" 3	4,300,000	5,600	48	41	5	6 20
" 4	4,000,000	5,000	32	62	4	2	...	-	-	nil
" 5	4,300,000	3,900	20	70	7	3	...	-	-	" "
" 6	4,350,000	3,800	19	77	3	1	...	-	-	" "
" 7	4,500,000	3,800	14	74	8	4	...	-	- 20
" 7	15	76	4	5	...	-	- nil
" 8	4,200,000	3,800	25	61	2	12	- 20
" 11	28	56	5	11	...	-	- nil
" 16	-	- 20
" 17	4,900,000	5,800	20	58	13	9	...	-	- nil
" 25	-	- 20
" 26	5,000,000	5,800	42	39	+ 37 nil
" 27	21	65	9	5	+ 1
" 28	19	57	10	14	...	-
" 31	28	47	8	17
Aug. 3	33	35	8	24	+ 1
" 6	+
" 8	29	50	10	11	-
" 11
" 14	22	44	9	22	+ 1

KITSAME 303.

Date. 1904.	R.B.C.	W.B.C.	Percentages.				H.B. per cent.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.		As ₂ O ₃ in mgs.
			P.N.	S.M.	L.M.	Eos.		Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.	
August 18	46	35	6	13	-	-	-
" 22	23	49	8	20	-	-	-
" 25	28	49	8	15	...	-	...	-	-	-
" 27	-	-	-
" 28	-	-	-
" 29	-	-	-
" 31	-	-	-
September 3	-	-	-
" 9	-	-	-
" 15	-	-	-
" 24	-	-	-
" 26	30	36	4	30	86	-	-	-
" 28	5,000,000	10,900	-	-	-
" 29	-	...	-	-	-
" 30	-	-	-
October 3	-	-	-
" 7	-	-	-
" 10	-	-	-
" 17	-	-	-
" 21	-	-	-
" 28	-	-	-
November 4	-	-	-

CASE 304. MANAWA. MALE. AGE 25.

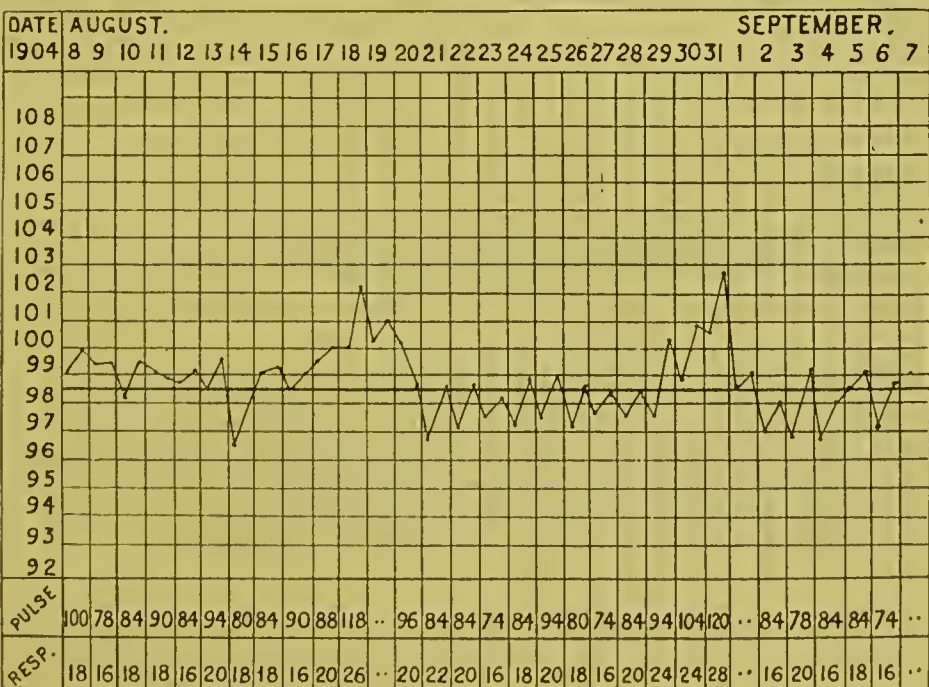
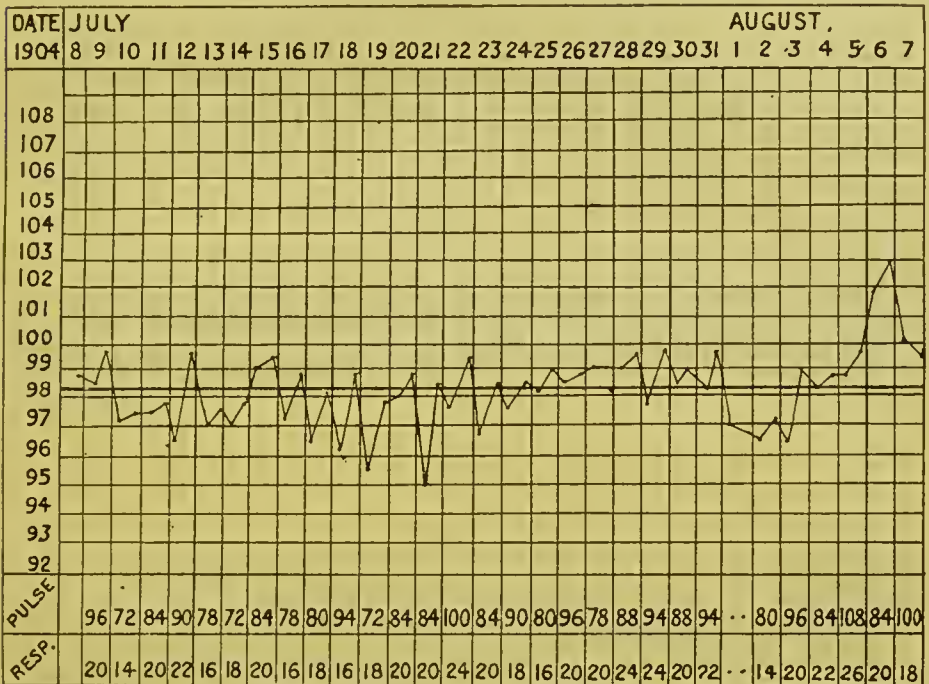
District. Usoga.

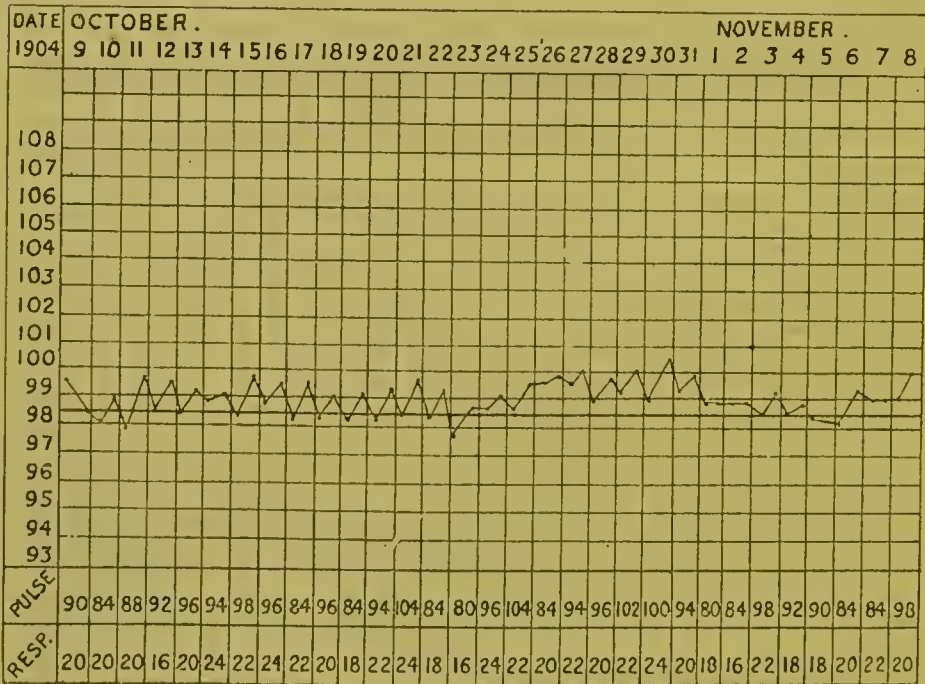
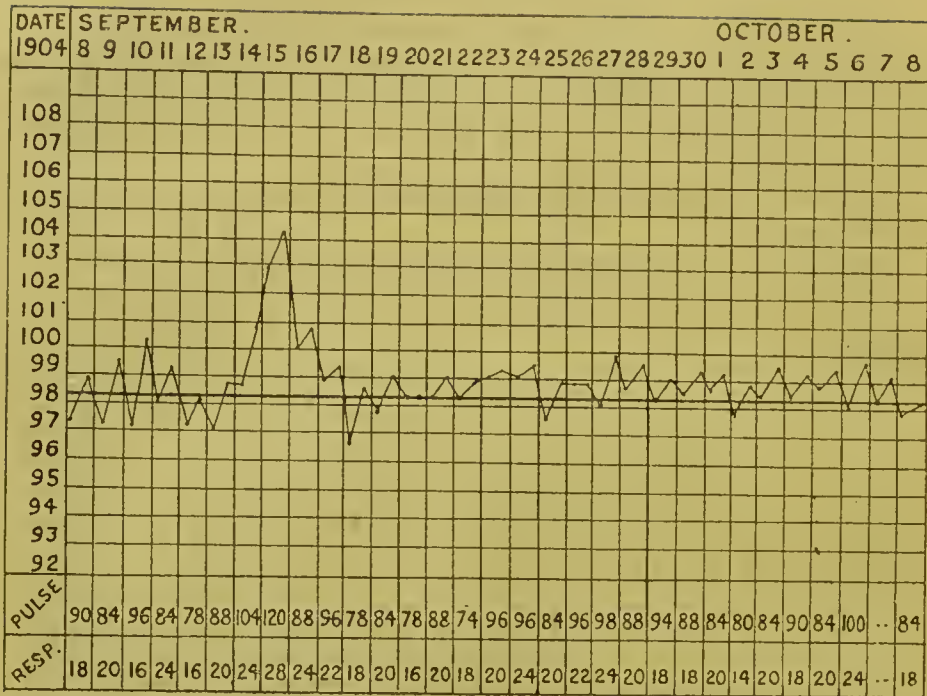
June 12, 1904. This man was also selected on account of enlarged glands in the neck. His general condition was good. The juice from a gland in the left posterior triangle of the neck was examined and was found to contain many active trypanosomes.

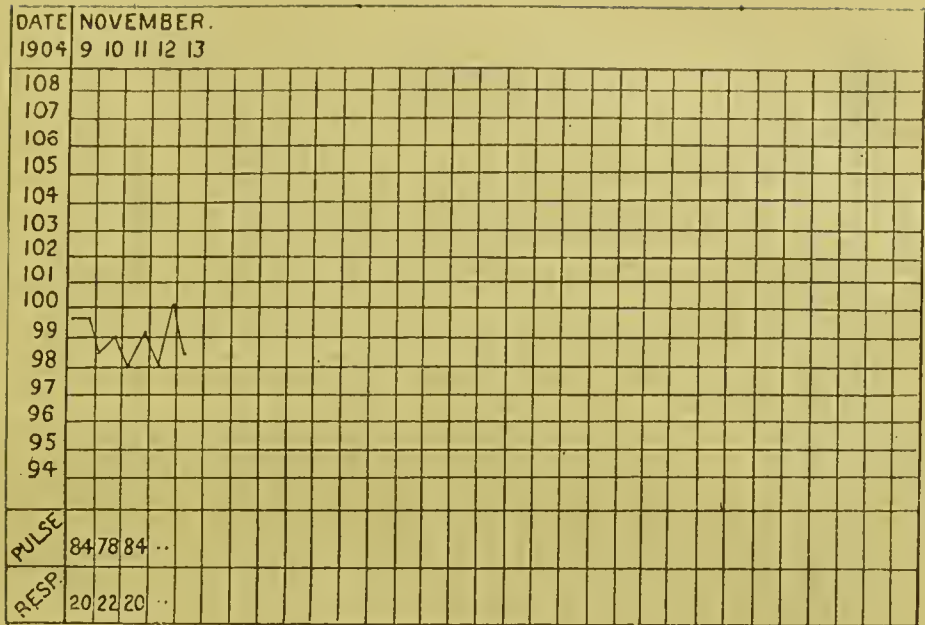
July 8. Intra-muscular injections of arsenious acid were commenced.

October 16. The general health of the patient is good.

The following chart shows the course of the disease :—







The following table shows the result of the enumeration of the blood corpuscles, the percentage of hæmoglobin, the amount of arsenious acid administered, the presence or absence of trypanosomes in the lymphatic glands, blood and cerebro-spinal fluid :—

Date. 1904.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.		As ₂ O ₃ in mgs.
			P.N.	S.M.	L.M.	Eos.		Strept.	Tryp.	Filar.	Malar.	Tryp.	Strept.	Tryp.	
June 12...	4,650,000	13,120	33	28	30	9	66	...	+	+	—	—	...	—	...
July 8...	4,500,000	11,200	24	44	15	17	78	...	+	+	—	—	10
" 9...	+	15
" 10...	4,800,000	11,870	33	41	18	8	78	...	+	+	20
" 11...	—	nil
" 12...	+ scanty	20
" 13...	—	20
" 16...	—	+	—	—	20
" 17...	4,600,000	9,100	28	63	6	3	80	+	—	—	nil
" 25...	4,500,000	7,500	15	69	8	8	80	+	—	—	"
" 31...	—	"
Aug. 6...	35	52	7	6	+	+	"
" 8...	11	69	13	7	+	+	"
" 11...	—	"
" 14...	32	52	6	10	—	"
" 18...	34	42	12	12	—	"
" 22...	+	—	—	"
" 25...	37	50	8	5	—
" 27...	—
" 28...	+	—	—
" 29...	+	—	—
" 31...	+	—	—
Sept. 3...	+	—	—

Date. 1904.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.		As ₂ O ₃ in mgs.
			P.N.	S.M.	L.M.	Eos.		Strept.	Tryp.	Filar.	Malar.	Tryp.	Strept.	Tryp.	
Sept. 9	+	-	Per cent.	nil
" 13...	+	-	-
" 15...	+	-	+
" 24...	+	-	-
" 26...	+	-	-
" 28...	5,000,000	12,500	19	58	11	12	88	+	-	-
" 29...	-	-	-
" 30...	-	-	-	-
Oct. 3	-	-	-
" 7	+	-	-
" 10	+	-	-
" 17	+	-	-
" 21	+	-	-
" 28	+	-	-
Nov. 4	+	-	-

CASE 310. MONDU. MALE. AGE 25.

District. Usoga.

July 8, 1904. This case was also selected from a group of prisoners. He had general enlargement of the superficial lymphatic glands, but no signs of sleeping sickness. The juice from a gland in the right posterior triangle of the neck was examined and found to contain many active trypanosomes.

July 10. Intra-muscular injections of arsenious acid were commenced.

October 10. The general health of the patient is good.

The temperature remained about normal. Occasional slight rises were associated with the presence of trypanosomes in the blood.

The following table shows the result of the enumeration of the blood corpuscles, the percentage of hæmoglobin, the amount of arsenic administered, the presence or absence of trypanosomes in the blood, lymphatic glands and cerebro-spinal fluid :—

Date. 1904.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.		As ₂ O ₃ in mgs.
			P.N.	S.M.	L.M.	Eos.		Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.	
July 9	5,200,000	8,700	47	28	5	10	85	-	+	+	-	Per cent.
" 10	+1	10
" 11	15
" 12	5,100,000	9,000	42	40	6	12	86	...	+	...	-	20
" 13	+	20
" 16	-	20
" 17	5,150,000	10,000	32	48	8	12	89	...	-	-	20
" 25	nil
" 26	5,000,000	6,000	14	60	8	18	85	nil
" 28	26	33	16	25	-	-	-
" 31
August 3	-	-	-	-
" 6	-	-	-	-
" 8	34	61	3	2	-	-	-	-
" 11	53	30	6	11	+1
" 14	44	37	7	12	+4
" 18	46	34	5	15
" 22	44	28	6	22
" 25
" 27	-
" 28
" 29	-	-
" 31	-	-
Sept. 3	-	-

Date.	R.B.C.	W.B.C	Percentages.				H.B. per cent.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.		As ₂ O ₃ in mgs.
			P.N.	S.M.	L.M.	Eos.		Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.	
September 9	+	+	Per cent.
" 13	+	+	-
" 15	+	+	-
" 24	+	+	-
" 26	+	+	-
" 28	5,300,000	11,600	33	48	10	9	96	+	+	-
" 29	+	+	-
" 30	+	+	-
October 3	+	+	+
" 7	+	+	+
" 10	+	+	+
" 17	+	+	+
" 21	+	+	+
" 28	+	+	+
November 4	+	+	+

CASE 311. NAMUTIDE. FEMALE. AGE 20.

Entebbe.

July 13, 1904. The patient came complaining of headache and fever. She states that she has been sick for six months. There is general enlargement of the superficial lymphatic glands, especially the cervical. A lymphatic gland in the left posterior triangle was punctured and the juice examined. It was found to contain many active trypanosomes.

The following table shows the result of the enumeration of the blood corpuscles, the percentage of hæmoglobin, the amount of arsenic administered, the presence or absence of trypanosomes in the blood, lymphatic glands and cerebro-spinal fluid:—

Date. 1904.	R.B.C.	W.B.C.	Percentages.				Parasites in glands.		Parasites in blood.			Parasites in C.S.F.		Hb. per cent.	As ₂ O ₃ . mgs.
			P.N.	S.M.	L.M.	Eos.	Strept.	Tryp.	Fil.	Mal.	Tryp.	Strep.	Tryp.		
July 13	4,400,000	15,000	33	40	7	20	-	+	10
" 14	15
" 15	4,500,000	10,000	25	45	8	22	-	-	20
" 16	20
" 17	4,600,000	7,000	26	49	9	16	20
" 19	4,400,000	6,870	33	42	7	18	...	-	20
" 21	4,200,000	9,300	42	44	2	12	20
" 23	4,050,000	8,400	30	44	6	20	...	-	20
" 26	4,000,000	8,700	11	64	6	19	nil
" 30	4,600,000	12,500	8	60	5	27	,
Aug. 4	4,350,000	7,500	11	75	2	12	"
" 6	31	44	12	13	"
" 8	4,800,000	6,250	16	59	6	19	...	-	"
" 11	10	57	8	25	"
" 14	"
" 15	5,000,000	9,300	34	44	5	18	...	-	"
" 20	18	47	8	27	"
" 23	5,100,000	30,000	33	36	3	28	"
" 29	5,000,000	13,700	"

As well as the cases above mentioned of trypanosoma fever, information has been got as to the after history of the men of the general population mentioned in the last Report in whose blood trypanosomes were found, but who, then, had no symptoms of sleeping sickness.

It has not been possible to trace out all these men owing to various causes, but the histories of a sufficient number have been obtained. Eighty natives were examined, and trypanosomes were found in the blood of twenty-three. Of these twenty-three, it has been ascertained that since that date, three have died of undoubted sleeping sickness, one ran away from his shamba and was reported to have died of sleeping sickness. Two died from pneumonia (one was almost certainly in an early stage of sleeping sickness), five are now in an early stage of sleeping sickness.

No information has been obtained in six cases. The remainder (6) do not as yet present definite signs of sleeping sickness. These observations strongly support the contention that the so-called trypanosoma fever is an early stage of sleeping sickness. Further, that this phase of the disease may be short or very prolonged, the development of the last stage being dependent on an extension of the invasion of the lymphatic system to the lymph spaces of the nervous system. It will be of considerable interest to follow the further history of the six men showing still no signs.

The following table shows the results of the investigations into the after history of the men harbouring the trypanosomes in their blood:—

Table giving the after-history of men in whose blood *trypanosomes* were found in June, 1903.

No.	Name.	Age.	Sex.	District and Chief.	Date of Examination of Blood for Trypanosomes.	After-history.
1	Mucase ...	25	M.	Nkumba, Subugwao.	Present, June 13, 1903.	Died of sleeping sickness on December 13, 1903.
2	Saulo ...	18	"	Mugema ...	Present, June 26, 1903.	Died of sleeping sickness under care of French Fathers at Kisubi, December 2, 1903.
3	Gabula ...	20	"	Entebbe, Subugwao.	Present, June 22, 1903.	Became sick in his shamba. Was turned out by his friends, who stated he had sleeping sickness. Ran away and died in January, 1904, of sleeping sickness in Kyagwe.
4	Kululwe ...	40	"	Entebbe, Mugema.	Present, June 22, 1903.	He had gone to Buse, but was brought in by Subugwao. He showed on February 18, 1904, marked enlargement of lymphatic glands in both posterior triangles of neck, also in anterior. Pulse 108. Coarse tremors of hands. He is probably in an early stage of sleeping sickness. He is kept under observation.
5	Mugwanjamba ...	"	"	Kagagara ...	Present, June 8, 1903.	He ran away to Bulamwezi. Definite information has so far not been got, but is reported to have died of sleeping sickness.

6	Buza	30	"	Buse Island, Mugema.	Present, June 27, 1903.	Examined on December 30, 1903. Facial ex- pression dull. Lumbar puncture performed, cerebro-spinal fluid contains no active trypano- somes. Patient was given ticket for future identification.
7	Kitungula	25	"	Semagale Is- land, Sese.	Present, June 16, 1903.	Mr. Savile reports, "He saw this man on May 4, 1900, and he is apparently well."
8	Tevamukopi..	...	35	"	Bunami Island, Sese.	Present, June 16, 1903.	Mr. Savile reports, "He saw this man in Sese, on May 4, 1904, and he is apparently well."
9	Tangamalala	...	25	"	Buse Island, Rasto.	Present, June 23, 1903.	Examined at Entebbe on December 30, 1903. He had no marked signs of sleeping sickness.
10	Wagononje	"	"	Sese Island ...	Present, June 12, 1903.	No information.
11	Sebolyamba	"	"	" ...	Present, June 13, 1903.	" "
12	Gummia	40	"	" ...	Present, June 16, 1903.	" "
13	Zwaka	23	"	Kome Island ...	Present, June 13, 1903.	Rev. H. T. C. Weatherhead, July, 1904, writes, "that this man had left the island a short time ago and was suffering from sleeping sickness."
14	Nutaba	24	"	Bugaba Island...	Present, June 13, 1903.	No information.
15	Sebaganga	30	"	Buse Island ...	Present, June 19, 1903.	" "

No.	Name.	Age.	Sex.	District and Chief.	Date of Examination of Blood for Trypanosomes.	After-history.
16	Nasago ...	30	M.	Buse Island	Present, June 23, 1903.	No information.
17	Sabakaki ...	20	"	"	Present, June 27, 1903.	He was examined at Entebbe on December 30, 1903. He did not present any marked signs of sleeping sickness.
18	Karala Barigi	30	"	Entebbe	Present, March 12, 1903.	Died on April 18, 1904, from pneumonia.
19	Kumsarsabba	25	"	"	Present, March 28, 1903.	Under observation. General health is fairly good. Temperature irregular.
20	Jordien Murjan	35	"	"	Present, March 31, 1903.	This man is now in an early stage of sleeping sickness. Trypanosomes in cerebro-spinal fluid.
21	Tabula*	25	"	"	Present, April 15, 1904.	Health is still good and patient is able to continue at his work. Trypanosomes not yet present in cerebro-spinal fluid.
22	Bara Risgallah	35	"	"	Present, April 21, 1904.	Died May 5, 1904, from pneumonia. Nervous system preserved for minute study.
23	J. M. (European)	...	"	"	Present, April 2, 1903.	

* *Vide* footnote, p. 39.

9. *Are these trypanosomes pathogenic to animals, and can any specific difference be made out between them by animal experiment?*

The experiments on the various animals have been continued throughout the year. The additional observations and results obtained strengthen and support the conclusions arrived at in the last report.

The monkey is the most satisfactory animal for experimental inoculation. The continued observations show that the effect produced in them is in all respects similar, whether the trypanosoma infection is produced by blood from so-called "trypanosoma fever" cases or the cerebro-spinal fluid of undoubted sleeping sickness cases. As the question of the relationship of these two morbid conditions is an important one, full details of the experiments are given.

The other animals that we have employed for experimental inoculation are dogs, jackals, cats, rats, guinea-pigs, rabbits, oxen, goats, sheep and donkeys. None of these have shown any marked susceptibility to the disease, and some have remained resistant.

- A. *Experiments on the effect on monkeys of the injections of cerebro-spinal fluid containing trypanosomes taken by lumbar puncture from cases of sleeping sickness.*

EXPERIMENT 2. MONKEY (MALE) (*Macacus Rhesus*).

March 23, 1903. Injected sediment of about 10 c.c. of cerebro-spinal fluid taken post-mortem from Case 18, Kaprec.

May 11. Injected 2 c.c. cerebro-spinal fluid.

May 21. Trypanosomes are found in the blood to-day, 10 days after the second inoculation.

August 25. No marked symptoms up to the present.

November 28. Animal has been getting distinctly emaciated. He looks ill, but is able to rise.

The temperature curve remained about normal from March till August, 1903. From September, 1903, the evening temperature rose to about 103°, 105°, and fell in the morning to about 100°. The day before death, December 2, 1903, it fell to 94·8°.

The following table shows the presence or absence of trypanosomes in the blood and cerebro-spinal fluid :—

Date. 1903.	Parasites in blood.				Parasites in C.S.F.	
	Filar.	Malar.	Tryp.	Strept.	Tryp.	Strept.
April 9	...	—	—
" 11	...	—	—
" 23	...	—	—
" 30	...	—	—
May 7	...	—	—
" 14	...	—	—
" 21	...	—	+
" 28	...	—	+
June 4	...	—	+
" 11	...	—	+
" 18	...	—	+
" 25	...	—	+
July 1	...	—	+
" 23	...	—	+
" 31	...	—	+
Aug. 7	...	—	+
" 13	...	—	+
" 20	...	—	+
" 27	...	—	—
Sept. 4	...	—	—
" 12	...	—	—
" 25	...	—	—
Oct. 9	...	—	+
" 22	...	—	—
Nov. 5	...	—	+
" 19	...	—	—
" 25	...	—	—
Dec. 3	...	—	+	...	—	...

December 3. Died. Post-mortem.

The body is rather emaciated, pupils equal and normal. Slight general enlargement of glands.

On opening the body there was some increase of pericardial fluid, no increase of fluid in pleural or peritoneal cavities.

Brain.—On removing the calvarium and reflecting the dura mater some congestion of surface is seen—no distinct flattening; cerebro-spinal fluid not increased; examination of fluid does not show any active trypanosomes.

Heart.—Muscle is rather pale. Blood examined microscopically from this organ in stained preparation, some structures, probably altered trypanosomes, were seen.

Lungs.—Right somewhat congested, no consolidation; left healthy.

Liver, spleen and kidneys.—Nothing noteworthy.

Lymphatic glands.—Enlarged.

Remarks.—This animal has not shown such pronounced drowsy symptoms as some have, but it has become distinctly emaciated. Some time before its death it was much less lively, and took no notice of people, and did not come forward readily for its food. The post-mortem showed nothing to account for death apart from the trypanosomes.

EXPERIMENT 34. MONKEY (MALE) (*Macacus Rhesus*).

To note the effect of injecting the cerebro-spinal fluid from a case of sleeping sickness into the vertebral canal of a monkey.

April 8, 1903. Injected 1 c.c. of cerebro-spinal fluid containing trypanosomes from a case of sleeping sickness into the spinal canal of this monkey.

April 30. Trypanosomes appeared in the blood to-day, 19 days after inoculation into the spinal canal. Note that the temperature curve shows no sign of this invasion.

May 2. Trypanosomes numerous in the blood. Temperature taken and found to be 106.4° F.

August 25. This monkey is beginning to show the usual symptoms of the disease in the monkey. He sits most of the day with his head fallen on his chest, evidently asleep, and his temperature has become very irregular.

The temperature remained normal till May 20, 1903. From that date it showed an evening rise averaging 103° – 104° . From August, 1903, the temperature remained sub-normal, falling to 94.2 on September 7, 1903, the day of its death.

The following table shows the presence or absence of trypanosomes in the blood and cerebro-spinal fluid:—

Date. 1903.	R.B.C.	W.B.C.	S.M.	L.M.	P.	Parasites in blood.				Parasites in C.S.F.	
						Filar.	Mal.	Tryp.	Strep.	Tryp.	Strep.
April 11	...	6,100,000	71	3	26	-	-	-
" 24	-	-	-
" 30	-	+
May 7	-	+
" 14	-	+
" 21	-	+
" 27	-	+
June 4	-	+
" 11	-	+
" 18	-	+
" 25	-	+
July 1	-	+
" 23	-	+
" 31	-	+
Aug. 13	-	+
" 20	-	+
" 27	-	+
Sept. 4	-	-
" 7	-	+	..	+	..

September 7. Has continued in the same condition since last note. He was in a dying state this morning. Killed by chloroform.

Post-mortem immediately after death.

The body is emaciated, coat very rough.

Brain.—On removing the calvarium and reflecting the dura mater some opacity of the membranes is seen, some flattening of the convolutions and slight adhesions at base of brain.

Fluid from the third ventricle was examined and active trypanosomes were seen. There was some blood in the fluid.

Heart.—Normal; blood taken from that organ showed the presence of trypanosomes.

Lungs.—A few pigmented areas, otherwise nothing noteworthy.

Liver.—Appears to be fatty.

Spleen.—Nothing noteworthy.

Kidneys.—Apparently healthy.

Lymphatic glands in mesentery and retroperitoneal regions were enlarged. Also those in inguinal region and left axilla.

Remarks.—This animal towards the end showed very characteristically the usual features of the disease met with in monkeys. The post-mortem appearances were also pretty typical of an ordinary sleeping sickness case. The trypanosomes were found living in the cerebro-spinal fluid.

EXPERIMENT 95. MONKEY (*Cercopithecus sp.*).

To note the effect of injecting the cerebro-spinal fluid from a case of sleeping sickness into the vertebral canal of a monkey.

May 13, 1903. Blood examined; there were no malarial parasites or trypanosomes present.

May 14. Injected 1 c.c. of cerebro-spinal fluid from a case of sleeping sickness into the vertebral canal of this monkey.

August 26. About 8.30 a.m. monkey had a convulsive seizure affecting the left side of its body. It lay on the ground for about an hour. Monkey appears rather crouched up.

August 29. Animal died this morning.

The following table shows the presence or absence of trypanosomes in the blood and cerebro-spinal fluid:—

Date. 1903.	Parasites in Blood.				Parasites in C.S.F.	
	Filar.	Mal.	Tryp.	Strep.	Tryp.	Strep.
May 13	...	—	—
" 22	...	—	—
" 29	...	—	—
June 4	...	—	+
" 11	...	—	—
" 20	...	—	+
" 25	...	—	+
July 1	...	—	+
" 23	...	—	—
" 31	...	—	+
Aug. 13	...	—	+
" 21	...	—	+
" 28	...	—	—
" 29	...	—	—	...	—	...

Post-mortem examination.

On removing the calvarium and reflecting the dura mater the convolutions were seen to be somewhat flattened. There was no marked congestion. The cerebro-spinal fluid was examined microscopically, but no living trypanosomes could be found.

Heart.—Nothing noteworthy—blood from this organ examined microscopically did not show the presence of trypanosomes.

Lungs.—Both showed the presence of infarctions.

Spleen.—Congested and somewhat enlarged.

Liver.—Nothing noteworthy.

Kidneys.—Both apparently healthy.

Remarks.—In this case the animal had a very definite involvement of the nervous system shortly before its death; probably due to interference with the cerebral circulation by the parasite. This condition no doubt caused the death of the animal. The absence of the parasites from the peripheral circulation just before death coinciding with the nervous seizure suggested their having lodged in the nervous system.

EXPERIMENT 96. MONKEY (*Cercopithecus sp.*).

To note the effect of injecting the cerebro-spinal fluid from a case of sleeping sickness into the vertebral canal of a monkey.

May 14, 1903. Blood examined—no malaria or trypanosomes.

Injected 1 c.c. of cerebro-spinal fluid from a case of sleeping sickness into the vertebral canal of this monkey.

August 25. No symptoms. No rise of temperature.

The following table shows the presence or absence of trypanosomes in the blood:—

Date. 1903.	Parasites in Blood.				Parasites in C.S.F.	
	Filar.	Mal.	Tryp.	Strep.	Tryp.	Strep.
May 14	+	—
„ 22	+	—
„ 29	+	—
June 4	+	—
„ 11	+	—
„ 20	+	—

June 24. Again injected 1 c.c. of cerebro-spinal fluid from a case of sleeping sickness into the spinal canal of this monkey.

October 29. Injected 5 c.c. of cerebro-spinal fluid from a case of sleeping sickness under the skin of this monkey.

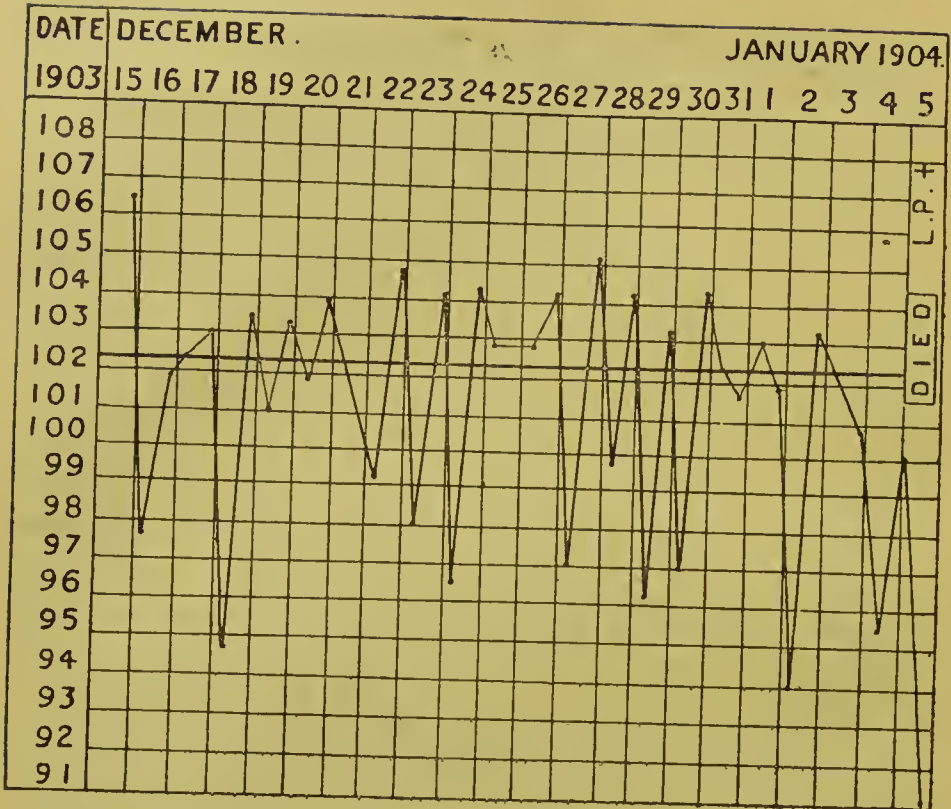
December 15. This monkey is getting thinner and is not so active, tending to sit crouched up. He is out of condition.

December 26. His attitude is now very characteristic. His head is drooping between his knees. He seldom raises his head, and if he does so it immediately falls again. He is unable to climb into his box without help.

January 1, 1904. Animal is very ill. Saliva is dribbling out of his mouth, and there appears to be some paresis of the muscles about his mouth.

January 5. He is now lying on his back. Breathing very shallow. Conjunctival reflex still present. Passing his motions under him. Closely resembles a case of sleeping sickness. Performed lumbar puncture; drew off 1 c.c. cerebro-spinal fluid. Microscopically shows some red and white cells and active trypanosomes.

The following chart represents the temperature curve. The observations were begun as soon as the animal was observed to be ill:—



The following table shows the presence or absence of trypanosomes in the blood and cerebro-spinal fluid:—

Date.	Parasites in blood.				Parasites in C.S.F.	
	Filar.	Malar.	Tryp.	Strept.	Tryp.	Strept.
1903.						
July 1	...	+	-
" 23	...	+	-
" 31	...	+	+
Aug. 13	...	+	+
" 21	...	+	+
" 27	...	+	+
Sept. 4	...	+	-
" 12	...	+	+
" 25	...	+	-
Oct. 8	...	+	-
" 22	...	+	-
Nov. 5	...	+	-
" 19	...	+	+
Dec. 3	...	+	-
" 18	...	+	+
" 26	...	+	+
1904.						
Jan. 1	...	+	+
" 5	...	+	+	...	+	...

January 5, died 12.30 p.m.

Post-mortem immediately after death.

The body is profoundly emaciated—sore over lumbar region; pupils are equal and normal. The inguinal, axillary and cervical glands are enlarged.

On opening the body there is some increase of fluid in the pericardial cavity.

No fluid in pleural or peritoneal cavities.

Heart.—Some jelly-like material round base. Petechiæ are seen on the papillæ under endocardium of left ventricle. Muscle is pale. Blood taken from it and examined microscopically shows many living trypanosomes, and some appear vacuolated.

Lungs.—Are both healthy.

Liver.—Nothing noteworthy.

Spleen.—Is enlarged, dark in colour.

Kidneys.—Right shows two areas of infarction. Left nothing noteworthy.

Intestines.—Appear healthy.

Lymphatic glands of omentum and along the aorta and pelvic vessels are enlarged and congested.

Brain.—On removing the calvarium there was some increase of cerebro-spinal fluid. The convolutions were congested and showed slight flattening. The brain and spinal cord were preserved for future examination.

Remarks.—This animal towards the close of his life developed a condition which represented very perfectly the signs met with in an ordinary case of sleeping sickness. The trypanosomes were present and active in the cerebro-spinal fluid before death. His attitude during life was exactly similar to that shown in photograph of Experiment 60. Report IV.

EXPERIMENT 54. MONKEY (*Cercopithecus* sp.).

To note the effect of injection of cerebro-spinal fluid containing trypanosomes, from a case of sleeping sickness, into the brain cavity of a monkey.

April 9, 1903. Injected 1 c.c. of cerebro-spinal fluid from a case of sleeping sickness into the brain cavity of this monkey through the foramen magnum.

August 25. No symptoms of sleeping sickness noted.

November 16. Injected 5 c.c. of cerebro-spinal fluid from a case of sleeping sickness subcutaneously.

December 15. Animal is seedy and not so active as before.

January 1, 1904. Monkey is getting thin. Facial expression is dulled.

January 24. Animal is tending to crouch and his attitude at times is very characteristic. Face is puffy.

January 25. Monkey is lying on the ground. Limbs appear partially paralysed. He can be roused. Breathing is shallow. Saliva is dribbling from his mouth.

The temperature remained normal till May 9, 1903. Up to December, 1903, the temperature was not recorded as the animal showed no signs of sickness. From December, 1903, it showed an evening rise averaging two or three degrees. On January 25, 1904 (the day of its death) it fell to 99°.

The following table shows the presence or absence of trypanosomes in the blood and cerebro-spinal fluid :—

Date.	Parasites in blood.				Parasites in C.S.F.	
	Fil.	Mal.	Tryp.	Strept.	Tryp.	Strept.
1903.						
April 11	...	—	—	—
" 23	...	—	—
" 30	...	—	+
May 7	...	—	+
" 14	...	—	+
" 21	...	—	+
" 28	...	—	+
June 4	...	—	—
" 11	...	—	+
" 18	...	—	+
" 25	...	+	+
July 1	...	—	+
" 23	...	—	+
" 31	...	—	+
August 13	...	—	—
" 20	...	—	+
" 27	...	—	—
Sept. 4	...	—	—
" 12	...	—	+
" 25	...	—	—
October 8	...	—	—
" 22	...	—	—
Nov. 5	...	—	—
" 19	...	—	—
Dec. 3	...	—	—
" 18	...	—	—
1904.						
January 1	...	—	+
" 9	...	—	+
" 15	...	—	—
" 20	...	—	—
" 23	...	—	—
" 25	...	—	+	...	—	...

January 25, 1904. Died at 5 p.m. Post-mortem at once.

The body is not much emaciated. Pupils are equal and normal. Glands show slight general enlargement. There is some increase of fluid in pericardial cavity, no increase in pleural or peritoneal cavities.

Brain.—On removing the calvarium and reflecting the dura mater, which was adherent in the frontal region on both sides, the convolutions were seen to be congested and showed slight

flattening. Brain was removed entire for minute examination, cerebro-spinal fluid examined microscopically did not show the presence of active trypanosomes.

Heart.—Some jelly-like material round base, otherwise nothing noteworthy. Blood from this organ examined microscopically did not show fully formed trypanosomes, but some bodies which were apparently broken down trypanosomes.

Lungs.—Both healthy.

Liver.—Slightly enlarged and congested.

Spleen.—Somewhat enlarged and firm on section.

Kidneys.—Both normal.

Lymph glands of mesentery and also along the side of great vessels are enlarged and congested.

Remarks.—In this animal the first apparent sign was a peculiar alteration of facial expression, the face was dull, puffy and wanting in brightness—a similar condition to that met with in sleeping sickness cases. He also tended to crouch up at the same time and finally assumed the usual characteristic attitude. A peculiar fact was that the trypanosomes which had been absent from the peripheral blood for a long period reappeared just before death.

There was no other cause discovered at the post-mortem to account for the animal's death apart from the trypanosomes.

EXPERIMENT 309. MONKEY (*Cercopithecus sp.*).

To note the effect of subcutaneous injection of gland juice from a case of sleeping sickness into a monkey.

June 30, 1904. Injected subcutaneously 0.5 c.c. of emulsion of cervical lymph gland from case of sleeping sickness into a monkey.

July 15. Trypanosomes present in the blood to-day, the fifteenth day after inoculation.

The following table shows the presence or absence of trypanosomes in the blood:—

Date.				Parasites in blood.		
				Fil.	Mal.	Tryp.
1904.						
July	2	—	—
"	15	—	+
"	22	—	+
"	30	—	+
August	5	—	+
"	12	—	+
"	26	—	+
Sept.	2	—	+
"	9	—	+

Date.				Parasites in blood.		
				Fil.	Mal.	Tryp.
Sept.	15	—	+
"	23	—	+
"	30	—	+
October	7	—	—
"	14	—	+
"	21	—	+
Nov.	4	—	+

Remarks.—This experiment is given to show that the gland juice as well as the cerebro-spinal fluid and blood of sleeping sickness cases when injected into a monkey can produce trypanosoma infection.

B. Experiments on the Effect of the Injection into Monkeys of Blood containing Trypanosomes from Cases showing no Symptoms of Sleeping Sickness.

EXPERIMENT 6. MONKEY (*Cercopithecus sp.*).

To note effect of injection of blood from Case 63, Kumsasaba.

March 28, 1903. Injected 4 e.c. blood from Dr. Baker's case, Kumsasaba, a policeman whose blood contained trypanosomes yesterday.

August 15. No symptoms.

January 28, 1904. Facial expression of this monkey is somewhat altered, being dull and heavy.

April 10. Removed 5 e.c. blood, also two enlarged glands from right femoral region. No active trypanosomes in the lymphatic juice.

April 18. Animal is very sick and is lying on the ground.

The temperature remained normal till August, 1903. From September, 1903, it showed a distinct evening rise of one or two degrees until the day of its death on April 18, 1904.

The following table shows the presence or absence of trypanosomes in the blood, lymphatic glands and cerebro-spinal fluid:—

Date.			Parasites in lymph glands.		Parasites in blood.				Parasites in C.S.F.	
			Tryp.	Strept.	Filar.	Malar.	Tryp.	Strept.	Tryp.	Strept.
1903.										
April	9	+	-
"	11	+	-
"	23	-	+	-
"	30	-	+	-
May	7	+	+
"	14	+	+
"	21	+	+
"	28	+	+
June	4	+	+
"	11	+	-
"	18	+	-
"	25	-	+
July	1	+	+
"	23	+	+
"	31	+	-
Aug.	7	+	+
"	13	+	-
"	20	+	+
"	27	+	-
Sept.	4	+	+
"	12	+	+
"	25	+	-
Oct.	8	-	+
"	22	+	+
Nov.	5	+	-
"	19	+	-
"	25	+	+
Dec.	3	+	-
"	18	+	+
"	31	+	-
1904.										
Jan.	9	+	+
"	15	+	+
"	28	+	+
Feb.	6	+	+
"	21	+	+
"	28	+	+
March	6	+	+
"	13	+	+
"	20	+	+
"	28	+	+
April	10	...	-	-	...	+	+
"	19	+	+	...	-	...

April 19. Died in the night. Post-mortem.

The body is not emaciated. Wound in right femoral region practically healed and quite healthy. Superficial glands are generally enlarged and somewhat congested.

On opening the body there is no increase of pericardial or pleural fluid, in the peritoneum there is some exudation of lymph surrounding the rectum and lower part of sigmoid flexure

of colon, this is firmly adherent to the bowel and is probably a few weeks old.

Brain.—On removing the calvarium and reflecting the dura mater the surface of the brain is pale, but shows nothing noteworthy to the naked eye. Spinal cord removed with roots and ganglion. Brain and spinal cord reserved for minute examination.

Heart.—Nothing noteworthy.

Lungs.—Both are somewhat congested.

Liver.—Apparently healthy.

Kidneys.—Nothing noteworthy.

Spleen.—Slightly enlarged.

Lymphatic glands.—Enlarged along aorta and iliac vessels.

Remarks.—Clearly in this experiment the course of the disease was interrupted by an intercurrent condition, the local peritonitis, which was undoubtedly occasioned by traumatism whilst introducing the thermometer into the rectum, assisted by the anæmia occasioned by the removal of 5 c.c. of blood, brought about prematurely the fatal issue. It is interesting to note the long duration of the disease in monkeys.

EXPERIMENT 58. MONKEY, BLACK-FACED VARIETY (*Cercopithecus sp.*).

April 21, 1903. Injected subcutaneously 3 c.c. of blood, containing trypanosomes from Case 68, Bara Risgallah.

April 30. Trypanosomes appeared in the blood to-day for the first time, nine days after injection.

August 20. Up to the present this monkey has shown no signs of being ill.

December 2. For the last few days animal has been very quiet and its head is constantly nodding. The grass has been allowed to grow round the foot of his box, indicating that for some time past he has been out of health.

December 3. Animal has now assumed a very characteristic attitude, crouching on the ground with his head between his knees—a typical picture of sleeping sickness as depicted in Experiment 60, Report IV.

December 6. Animal is now lying on his side unable to rise. He is in a lethargic condition, apparently dying. Lumbar puncture at 2 p.m., a few drops of clear fluid obtained—showed under the microscope a few red cells and active trypanosomes. Breathing regular. Heart sounds very weak. Died at 5 p.m.

The temperature shortly before death fell considerably below normal.

The following table shows the presence or absence of trypanosomes in the blood and cerebro-spinal fluid:—

Date.	Parasites in blood.				Parasites in C.S.F.	
	Filar.	Malar.	Tryp.	Strep.	Tryp.	Strepto.
1903.						
April 14	+	—
" 30	+	+
May 7	+	+
" 14	+	+
" 21	+	+
" 28	+	+
June 4	+	+
" 11
" 18	—	+
" 25	—	+
July 1	—	+
" 23	+	+
" 31	+	+
Aug. 13	—	+
" 20	—	+
" 27	—	+
Sept. 4	—	+
" 12	—	+
" 25	+	+
Oct. 8	—	+
" 22	—	+
Nov. 5	+	—
" 19	—	—
Dec. 3	—	+
" 6	+	+	...	+	...

Post-mortem examination after one hour.

External appearances.—Animal is not emaciated. Slight general enlargement of lymphatic glands. Pupils normal.

Chest.—No increase of pericardial or pleural fluid.

Heart.—Some jelly-like material round the base, otherwise normal.

Lungs.—Nothing noteworthy.

Abdomen.—No increase of peritoneal fluid.

Liver, spleen, and kidneys.—Are all healthy.

Lymphatic glands in mesentery are enlarged.

Brain.—The surface is somewhat dry, with slight flattening of the convolutions and no increase of cerebro-spinal fluid. Brain removed entire for minute investigation. Spinal cord shows naked eye nothing noteworthy; kept for microscopic examination. Smears of heart's blood show the presence of trypanosomes; they are few in number and peculiarly altered, being very like those depicted in Experiment 60. Malaria is also present.

Remarks.—This experiment is a most important one, as affording proof of the identity of the trypanosoma of sleeping sickness and that found in men in their lymphatic glands and blood. Towards the end the animal presented a picture of a sleeping sickness case in its last stages; the mode of death being also similar, viz., lying in a state of torpor with sub-normal tempera-

ture. The presenee of trypanosomes in the cerebro-spinal fluid obtained by lumbar puncture was very suggestive. The long duration of the experiment also brings it closely into line with the condition found in sleeping sickness, and this condition was produced by a single injection of blood from Experiment 68, Bara Risgallah. There was no other cause to account for the animal's death apart from the trypanosomes.

EXPERIMENT 123. MONKEY (*Cercopithecus sp.*).

To note the effect of blood containing trypanosomes from Case 64, Jordien Murjan.

May 25, 1903. Examined blood. No trypanosomes present. Injected 1 c.c. of blood from Case 64, Jordien Murjan, into the brain of this monkey.

November 9. Injected under the skin 10 c.c. blood from Jordien Murjan.

December 31. Animal appears seedy. He tends to crouch and is not taking his food.

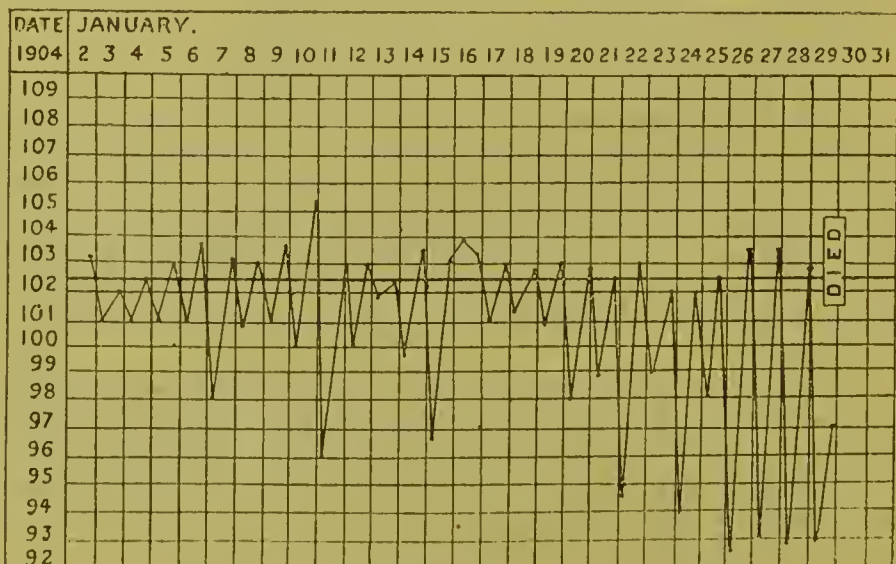
January 9, 1904. Drew off 2 c.c. cerebro-spinal fluid by lumbar puncture but found no living trypanosomes in it.

January 22. Condition is quite typical of sleeping sickness met with in monkeys. He is very thin.

January 24. Somewhat peculiarly altered trypanosomes seen in the blood.

January 29. Animal very sick to-day. Attitude quite typical. General tremors of his body. Eyes are shut as if asleep. He can be roused, but his head immediately droops between his legs and his eyes shut. Has a very drowsy look. 4 c.c. cerebro-spinal fluid removed by lumbar puncture; no active trypanosomes seen.

The following chart shows the temperature curve:—



The following table shows the presence or absence of trypanosomes in the blood and cerebro-spinal fluid:—

Date.	Parasites in blood.			Parasites in C.S.F.	
	Filar.	Mal.	Tryp.	Tryp.	Strept.
1903.					
May 25	...	—	—
" 28	...	+	—
June 4	...	+	—
" 11	...	+	+
" 20	...	+	+
July 1	...	+	+
" 23	...	+	+
" 31	...	+	+
Aug. 13	...	—	+
" 21	...	+	+
" 28	...	+	+
Sept. 4	...	+	+
" 12	...	+	+
" 25	...	+	—
Oct. 8	...	+	—
" 22	...	+	—
Nov. 5	...	+	—
" 19	...	+	—
Dec. 3	...	+	—
" 13	...	+	—
" 18	...	—	—
" 31	...	—	—
1904.					
Jan. 9	...	—	—	—	...
" 15	...	—	—
" 24	...	—	+
" 27	...	—	—
" 29	...	—	—	—	...

January 29. Died at 6 p.m. Post-mortem at once.

The body was profoundly emaciated. Glands show slight general enlargement. Pupils equal and normal. No sores. No increase of fluid in pericardial or pleural cavities, slight increase in peritoneal cavity.

Brain.—On removing the calvarium and reflecting the dura mater the superficial vessels are seen to be congested. Slight flattening of the convolutions, some increase of sub-arachnoid fluid. Examination of cerebro-spinal fluid on day of death showed no living trypanosomes. Brain removed entire for minute investigation.

Heart.—No noteworthy change. Blood removed from it showed no trypanosomes.

Lungs.—Both healthy.

Liver.—Healthy.

Spleen.—Nothing noteworthy.

Kidneys.—Both normal.

Glands.—Enlarged in mesentery—some are congested.

Remarks.—Towards the end this monkey presented a most striking clinical picture of a sleeping sickness case. The attitude, the general tremors of the body, the swinging temperature, were all very marked. The blood with which this animal was injected was obtained from a case which is, now, in the earliest stage of sleeping sickness. The trypanosomes were at one time very numerous in the blood; after being absent on several occasions they reappeared in the blood and were scanty and somewhat altered. The lymphatic glands were not examined *intra vitam* or *post-mortem*. Had they been examined it is possible living trypanosomes would have been found.

There is no doubt this animal died from trypanosoma infection, as there was nothing else to account for death. A similar disappearance of the trypanosomes from the peripheral blood was met with in the animal varieties; compare Experiment 179 (mule) and Experiment 152 (Pordage's ox).

EXPERIMENTS ON THE EFFECT OF THE INJECTION OF THESE TRYPANOSOMES INTO DOGS.

As stated in the Further Report, the native dog of Uganda is not satisfactory as an experimental animal. The majority die of anchylostomiasis before the experiment is finished.

The pup appears to be distinctly less susceptible than the adult. Both of the pups became infected by *piroplasma canis*, which also occurred amongst other dogs in Entebbe. It is probably conveyed by means of a tick. This parasite was further studied. A jackal was also inoculated with blood containing *Trypanosoma gambiense*. The course of the disease was similar to that in the adult dog. Its susceptibility is not so great as the monkey, but greater than the goat. This gradation of susceptibility is also seen amongst men: in the table giving the after-history of the cases in which trypanosomes were present in the blood only a year ago, it will be observed that some cases rapidly passed into the sleeping sickness stage and died, others took much longer and some appeared quite well about a year later. It is possible that some of these are refractory.

EXPERIMENT 144. BRINDLED PUP.

To note effect of subcutaneous injection of cerebro-spinal fluid containing trypanosomes from a case of sleeping sickness into a pup.

June 23, 1903. Injected 4 c.c. cerebro-spinal fluid containing trypanosomes into this pup.

September 1. Again injected 4 c.c. cerebro-spinal fluid from case of sleeping sickness.

September 7. Injected 4 c.c. of cerebro-spinal fluid from case of sleeping sickness.

September 14. Injected 8 c.c. of cerebro-spinal fluid from case of sleeping sickness.

September 29. Blood examined and pyrosoma canis was observed to be present.

October 1. Blood very pale. At 4 p.m. animal passed a little urine; examined spectroscopically showed the presence of hæmoglobin.

The temperature fell to 101° on October 1, 1903.

The following table shows the number of red cells, the percentage of hæmoglobin and the presence or absence of pyrosomes and trypanosomes in the blood:—

Date.	R.B.C.	Hb. per cent.	Parasites in the blood.				
			Filar.	Malar.	Pyro.	Tryp.	
1903.							
June 30	—	
July 17	—	
" 21	—	
" 28	—	
Aug. 4	—	
" 14	—	
" 18	—	
" 25	—	
Sept. 1	—	
" 8	—	
" 22	—	
" 29	+	—	
Oct. 1	1,600,000	15	+	—	

October 3. Post-mortem.

The body is fairly well nourished. Superficial glands not enlarged. On opening the body there is no increase of fluid in the pericardial, pleural or peritoneal cavities.

Heart.—Appears to be normal.

Lungs.—Both show minute embolic areas.

Liver.—Somewhat enlarged and apparently fatty.

Spleen.—Considerably enlarged, measures 7 inches by 2 inches.

Kidneys.—Both distinctly congested, especially the cortex and surface.

Bladder.—Contained some reddish brown urine.

Remarks.—In this experiment, although repeated injections of cerebro-spinal fluid were made, the animal remained completely refractory. In this animal the pyrosoma canis developed, and gave rise to all the usual signs of this disease as met with in dogs.

EXPERIMENT 146. BLACK PUP.

June 23, 1903. Injected subcutaneously 4 c.c. of blood from Case 64, Jordien Murjan, into this dog.

September 21. Again injected 5 c.c. of blood from Case 64, Jordien Murjan.

September 26. *Pyrosoma eanis* observed in the blood. Blood is very pale and watery.

October 13. Dog is out of condition—no dark urine noted.

November 3. Has been lying about lately, during night he passed smoky urine. This showed a hæmoglobin band on spectroscopic examination. Considerable quantity of albumen present.

The temperature remained about normal until November 5, 1903 (the day of death), when it fell to 93·2.

The following table shows the presence or absence of pyrosomes and trypanosomes in the blood:—

Date.				Parasites in the blood.			
				Filar.	Malar.	Pyrosoma.	Tryp.
1903.							
June 30...	—
July 17...	—
„ 21...	—
„ 28...	—
Aug. 4...	—
„ 14...	—
„ 18...	—
„ 25...	—
Sept. 1...	—
„ 8...	—
„ 15...	—
„ 22...	—
„ 29...	+	—
Oct. 1...	+	—
„ 2...	+	—
„ 4...	+	—
„ 6...	+	—
„ 7...	+	—
„ 8...	+	—
„ 12...	+	—
„ 26...	+	—
Nov. 3...	+	—

November 5. Post-mortem.

The body is fairly well nourished. No enlargement of superficial glands. No increase of fluid in pericardial, pleural or peritoneal cavities.

Heart.—Nothing noteworthy.

Lungs.—Both show areas of embolism. Examination of these microscopically shows many red cells infected with pyrosomes.

Liver.—Congested.

Spleen.—Distinctly enlarged, measures 10 inches by $2\frac{1}{2}$ inches. Microscopically shows corpnsceles infected with pyrosomes.

Kidneys.—Naked eye show nothing noteworthy. Capsule strip readily.

Bladder.—Contains urine which on examination shows the presence of blood.

Remarks.—This experiment shows that the young dog is absolutely refractory to the *Trypanosoma gambiense*, although the experiment lasted nearly 5 months. It was of interest further, in that the pyrosoma canis developed in it. This was one of a number of animals in Uganda in whom this parasite was discovered. Some inoculations were made to determine the effects on different animals of this parasite.

EXPERIMENT 151. JACKAL.

To note the effects of subcutaneous injection of blood from a man not showing signs of sleeping sickness into a jackal.

July 24, 1903. Injected subcutaneously 4 c.c. blood from Case 31, Karala Barigi.

November 2. This animal killed and almost entirely consumed a monkey, Experiment 232, in whose blood trypanosomes of the animal variety were abundantly present.

November 3. Blood of animal contains many trypanosomes.

The following table shows the presence or absence of trypanosomes in the blood:—

Date.				Parasites in the blood.		
				Filaria.	Malaria.	Trypanosoma.
1903.						
July	24	—
Aug.	4	+
"	18	+
"	25	—
Sept.	1	+
"	8	—
"	22	+
"	29	—
Oct.	13	—
"	27	—
Nov.	3	+

Remarks.—This experiment shows that the effects produced in an adult jackal by the *Trypanosoma gambiense* are practically the same as in the adult dog. The animal is only partially susceptible. The invasion of the other trypanosoma following

the eating of the monkey was undoubtedly, due to the animal having punctured itself with the bones, and in this way became infected with a variety of trypanosoma to which it is susceptible.

EXPERIMENT 198. CAT (FULL GROWN).

To note the effect of subcutaneous injection of blood from a case of trypanosoma fever into a cat.

September 23, 1903. Injected subcutaneously to-day 10 c.c. of blood from case of trypanosoma fever, Karala Barigi.

November 11, 1903. Again injected 8 c.c. of blood from case of trypanosoma fever, Karala Barigi.

January 19, 1904. Trypanosomes appeared in the blood to-day, 69 days after second injection.

The following table shows the presence or absence of trypanosomes in the blood:—

Date.				Parasites in the blood.		
				Filaria.	Malaria.	Trypanosoma.
1903.						
Sept.	23	—	—	—
"	30	—	—
Oct.	3	—	—
"	10	—	—
"	15	—	—
"	20	—	—
"	27	—	—
Nov.	3	—	—
"	11	—	—
"	17	—	—
"	24	—	—
Dec.	1	—	—
"	15	—	—
"	29	—	—
1904.						
Jan.	12	—	—
"	19	—	+
"	26	—	+
Feb.	2	—	+
"	9	—	—
"	16	—	+
"	23	—	+
Mch.	1	—	—
"	8	—	—
"	15	—	+
"	22	—	—
"	29	—	—
April	5	—	+
"	12	—	—
"	17	—	—
"	26	—	—

Date.	Parasites in the blood.		
	Filaria.	Malaria.	Trypanosoma.
May 3	...	—	+
" 10	...	—	+
" 17	...	—	—
" 31	...	—	—
June 14	...	—	—
" 21	...	—	—
" 28	...	—	—
July 12	...	—	—
" 19	...	—	—
" 26	...	—	—
Aug. 2	...	—	—
" 16	...	—	—
" 23	...	—	—
" 30	...	—	—
Sept. 3	...	—	—

September 3, 1904. The animal died to-day. It had been partially devoured by another eat. The general condition good. Superficial glands are not enlarged. Coat is in good order. No opacity of corneæ. No oedematous swellings. No increase of fluid in the pericardial, pleural or peritoneal cavities.

Heart.—Shows nothing noteworthy. The examination of the blood from this organ shows no trypanosomes.

Lungs.—Both healthy.

Liver.—Rather pale, otherwise healthy.

Kidneys.—Pale, otherwise both healthy.

Lymphatic glands.—Are not enlarged.

Remarks.—This experiment illustrates the course of the disease in the eat. Like the dog this animal shows a very slight susceptibility, the trypanosome tending to die out after being in the blood for a short time. This animal probably died from the effects of traumatism.

EXPERIMENT 308. CAT, YOUNG.

To note the effect of subcutaneous injection of blood from a case of sleeping sickness into a young eat.

June 23, 1904. Injected subcutaneously 2.5 e.e. of blood from a case of sleeping sickness. The blood contained numerous active trypanosomes.

July 12. Injected subcutaneously 3.5 e.e. of blood from same case of sleeping sickness.

July 26. Trypanosomes were found in the blood for the first time the 14th day after 2nd injection.

The following table shows the presence or absence of trypanosomes in the blood:—

Date.				Parasites in the blood.		
				Malar.	Filar.	Tryp.
1904.						
June	28	—
July	12	—
"	19	—
"	26	+
Aug.	2	+
"	9	+
"	16	+
"	23	+
"	30	+
Sept.	6	+
"	13	+
"	27	—
Oct.	4	—
"	11	—

Remarks.—This experiment shows that the eat can be infected with the trypanosoma derived from a case of sleeping sickness. Experiment 198 shows that the eat was susceptible also to the infection by the trypanosoma derived from the blood of a man showing no signs of the disease.

On the effect of the injection of these Trypanosomes into Guinea-pigs, Donkeys, Oxen, Sheep and Goats.

EXPERIMENT 82. GUINEA PIG.

To note the effect of subcutaneous injection of cerebro-spinal fluid containing trypanosomes from a case of sleeping sickness into guinea pig.

May 5, 1903. Injected 5 e.e. of cerebro-spinal fluid containing trypanosomes into this guinea pig subcutaneously.

September 1, 1903. Injected 2 e.e. cerebro-spinal fluid from case of sleeping sickness subcutaneously.

August 18, 1904. Injected 3 e.e. of cerebro-spinal fluid from case of sleeping sickness. The cerebro-spinal fluid contained many active trypanosomes.

Trypanosomes remained absent from the blood of this animal until after the third injection. They were first observed in the blood on October 4 and continued present.

Remarks.—In this guinea pig also trypanosomes have appeared in the blood, thus showing that the guinea pig is not absolutely refractory.

EXPERIMENT 81. GUINEA PIG (FEMALE).

To note the effect of subcutaneous injection of blood containing trypanosomes from man showing no signs of sleeping sickness into a guinea pig.

May 1, 1903. Injected $\frac{1}{2}$ c.c. of blood from Case 66, Jordien Murjan, containing trypanosomes.

September 21. Injected 5 c.c. of blood from Jordien Murjan subcutaneously.

June 23. Injected 2.5 c.c. blood from case of sleeping sickness. The blood contained trypanosomes.

No trypanosomes were found in the blood up to June 28, 1904.

The following table shows the presence or absence of trypanosomes in the blood after that date:—

Date.					Parasites in the blood.		
					Filar.	Malar.	Tryp.
July	12	—
"	26	—
Aug.	2	+
"	4	+
"	9	—
"	16	+
"	23	+
"	30	+
Sept.	6	+
"	13	+
"	27	+
Oct.	4	+
"	11	+
"	18	+
Nov.	2	+

Remarks.—In this case the trypanosomes appeared in the blood after repeated injections; the blood used in the last injection contained a very large number of trypanosomes.

EXPERIMENT 306. GUINEA PIG.

To note the effect of subcutaneous injection of blood containing trypanosomes from a case of sleeping sickness into a guinea pig.

June 23, 1904. Injected 2.5 c.c. of blood from a case of sleeping sickness. The blood contained many trypanosomes.

July 12. Injected 3 c.c. of blood from a case of sleeping sickness. The trypanosomes were numerous in the blood injected.

No trypanosomes were found in the blood of this animal at any time during the course of the disease.

EXPERIMENT 101. DONKEY.

To note the effect of subcutaneous injection of blood containing trypanosomes from man showing no obvious signs of sleeping sickness into donkey.

May 11, 1903. Examined blood. No trypanosomes. No malaria.

May 15. Injected 10 c.c. blood from Case 68, Bara Risgallah, into this donkey.

May 26. Again injected 10 c.c. blood from Case 68.

May 27. To-day large swelling was noticed in the region of the second injection.

June 5. Abscess opened; several ounces of pus evacuated.

September 21. Again injected with 10 c.c. blood from case Jordien Murjan.

No trypanosomes were found in the blood of this animal at any time during the course of the disease.

October 13. The blood of this animal never having shown the presence of trypanosomes even after injection of blood, it was tested with one of the animal varieties of trypanosomes, vide Experiment 229.

EXPERIMENT 312. DONKEY.

To note the effect of subcutaneous injection of blood containing trypanosomes from a case showing no signs of sleeping sickness into a donkey.

August 6, 1904. Injected subcutaneously 7 c.c. of blood from Case 304, Manawa. The blood contained numerous active trypanosomes.

August 18. Again injected 10 c.c. of blood.

No trypanosomes were found in the blood of this animal at any time during the course of the disease.

EXPERIMENT 305. DONKEY.

To note the effect of subcutaneous injection of cerebro-spinal fluid from a case of sleeping sickness into a donkey.

June 15, 1904. Injected 2 c.c. of cerebro-spinal fluid from a case of sleeping sickness. The cerebro-spinal fluid contained many active trypanosomes.

July 15. Injected 4 c.c. of cerebro-spinal fluid from a case of sleeping sickness.

The trypanosomes were never found in the blood of this animal at any time.

EXPERIMENT 132. OX, SMALL YELLOW.

June 17, 1903. Blood examined, trypanosomes absent.

June 21. Injected subcutaneously 10 c.c. of cerebro-spinal fluid containing trypanosomes from a case of sleeping sickness into this ox.

August 25. Injected subcutaneously 10 c.c. of cerebro-spinal fluid from case of sleeping sickness.

September 1. Again injected subcutaneously 10 c.c. of cerebro-spinal fluid into this ox.

September 14. Injected subcutaneously 10 c.c. of cerebro-spinal fluid from case of sleeping sickness.

June 15, 1904. Injected subcutaneously 4 c.c. of cerebro-spinal fluid containing many trypanosomes from a case of sleeping sickness.

August 18. Injected subcutaneously 10 c.c. of cerebro-spinal fluid containing many trypanosomes.

No trypanosomes were ever detected in the blood of this animal.

EXPERIMENT 148. OX.

July 1, 1903. Blood examined, trypanosomes absent.

July 22. Injected subcutaneously 10 c.c. of blood from Case 64, Jordien Murjan, into this ox.

September 21. Again injected subcutaneously 5 c.c. of blood containing active trypanosomes from Jordien Murjan.

September 23, 1904. Injected subcutaneously 7 c.c. of blood from Case 304, Manawa. The blood contained many active trypanosomes.

Trypanosomes were never detected in the blood of this animal at any time.

EXPERIMENT 89. SHEEP, BROWN.

To note the effect of subcutaneous injection of cerebro-spinal fluid containing trypanosomes from a case of sleeping sickness into a sheep.

May 11, 1903. Injected 10 c.c. of cerebro-spinal fluid containing trypanosomes from a case of sleeping sickness into this sheep.

June 30. Again injected 10 c.c. of fluid.

August 25. 10 c.c. of cerebro-spinal fluid injected.

September 1. 10 c.c. of cerebro-spinal fluid injected.

September 14. 10 c.c. of cerebro-spinal fluid injected.

June 15, 1904. Injected 2 c.c. of cerebro-spinal fluid containing many trypanosomes.

July 15. Injected 4 c.c. of cerebro-spinal fluid containing many trypanosomes.

August 18. Injected 6 c.c. of cerebro-spinal fluid containing many trypanosomes.

Trypanosomes were never found in the blood of this animal. The blood was examined weekly.

Remarks.—Although repeated injections of the fluid were made in this case, yet the trypanosomes have never appeared in the blood of the animal.

EXPERIMENT 149. SHEEP, SMALL BROWN AND WHITE.

To note effect of subcutaneous injection of blood containing trypanosomes from a man showing no obvious signs of sleeping sickness into sheep.

June 25, 1903. Injected subcutaneously 5 c.e. blood from Case 63, Kumsarsabba, containing active trypanosomes.

September 23. Again injected 10 c.c. blood subcutaneously from case Karala Bariji.

Trypanosomes were never found in the blood of this animal. The blood was examined weekly.

November 12. Sheep died this afternoon. Post-mortem.

The body was not emaciated.

Heart.—Fat about base partially absorbed. Blood very pale.

Lungs.—Nothing noteworthy.

Liver, Spleen and Kidneys.—Showed no naked eye change.

Remarks.—This animal never showed the trypanosomes in his blood. It was inoculated on two occasions with blood.

EXPERIMENT 90. GOAT.

To note effect of subcutaneous injection of blood containing trypanosomes from a man showing no signs of sleeping sickness into a goat.

May 11, 1903. Injected subcutaneously 5 c.e. of blood from Case 64, Jordien Murjan, containing trypanosomes, into this goat.

September 23. Injected subcutaneously 10 e.e. of blood from Case 63, Karala Bariji.

June 23, 1904. This animal having never shown trypanosomes in the blood, 5 e.e. of blood from a sleeping sickness case was injected subcutaneously.

July 15. Trypanosomes have not appeared in the blood, 4 e.c. of cerebro-spinal fluid from a case of sleeping sickness was injected.

August 18. Again injected 6 e.e. of cerebro-spinal fluid containing many active trypanosomes from a case of sleeping sickness.

August 31. Trypanosomes appeared in the blood to-day, thirteenth day after last inoculation.

Trypanosomes were once found in the blood of this animal.

Remarks.—This animal has shown trypanosomes in the blood. It would appear, therefore, that the goat is to a very

slight extent susceptible to infection by *Trypanosoma gambiense*.

EXPERIMENT 313. GOAT.

To note the effect of subcutaneous injection of blood containing trypanosomes from a case showing no signs of sleeping sickness into a goat.

August 6, 1904. Injected 5 c.c. of blood from Case 304, Manawa. The blood contained numerous active trypanosomes.

Trypanosomes were never found in the blood of this animal.

EXPERIMENT 152. MR. PORDAGE'S OX.

June 3, 1903. Found trypanosomes in blood. Injected dog, Experiment 128.

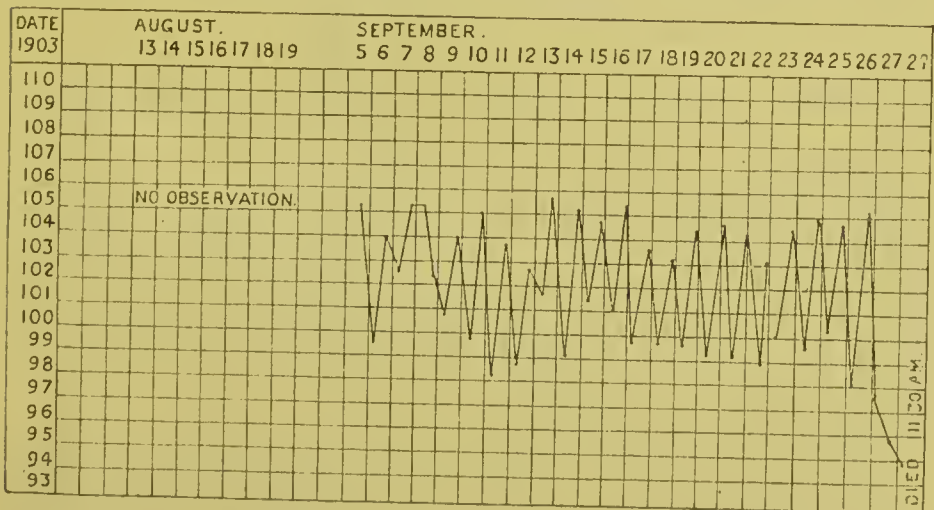
August 13. We received this ox from Mr. Pordage. It is merely a hide-bound skeleton.

August 16. No trypanosomes found in films, but in numbers after centrifuging. Again injected blood into dog, Experiment 128.

September 5. Animal is getting gradually thinner. The superficial lymphatic glands are greatly enlarged. About 30 c.c. of blood drawn off and examined after centrifuging, but no trypanosomes were found.

September 28. Animal was unable to walk. The temperature fell to 94.6. He died at 11.30 a.m.

The following chart represents the course of the fever for about one month before death.



Date.	Parasites in the blood.		
	Filar.	Malar.	Tryp.
1903.			
June 3	+
Aug. 16	+
" 19	+
Sept. 5	-
" 16	-
" 28	-

September 28. Died at 11.30 a.m. Post-mortem.

The body is profoundly emaciated. The superficial glands were generally enlarged and on section distinctly congested. A little jelly-like material present in subcutaneous tissue. Left cornea showed some opacity, none of right.

On opening the body, a little clear fluid escaped from the pericardial cavity—no increase of fluid in pleural or peritoneal cavities.

Heart.—Pale, shows yellow jelly-like material round base. Two small petechiæ seen under endocardium of left ventricle.

Lungs.—Both healthy.

Liver.—Contained two flukes, otherwise healthy.

Spleen.—Somewhat enlarged.

Kidneys.—Pale, otherwise nothing noteworthy.

Glands.—Retroperitoneal and mesenteric were enlarged.

Remarks.—This variety of trypanosoma more closely approaches the *Trypanosoma gambiense* than the other animal varieties which we have investigated in Uganda. Dogs are very susceptible to the other animal varieties, but proved refractory when inoculated with this variety.

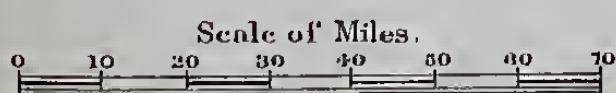
10. Further Observations on the Distribution of *Glossina palpalis*.

Since the last report, further observations have been made on the distribution of the fly and sleeping sickness. The results of these additional observations have been added to the maps of the distribution given in the Further Report, which have been extended in order to embrace them. Its occurrence round Lake Albert is interesting and important. In the light of this discovery, additional significance was given to a case of sleeping sickness coming from this district. The following are the chief points in the case:—

The patient was a Swahili sailor, named Sururu Bin Mze, who was employed on the Government boat running between Butiaba and Wadelai. Two years ago he came from Mombasa, and passed through Entebbe, remaining there for a day only, and then proceeded direct to Lake Albert. He remained at his work for two years; being then time-expired, he was discharged. On the journey to Entebbe he became ill, and when admitted

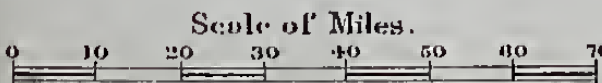
MAP SHOWING THE DISTRIBUTION OF GLOSSINA PALPALIS.

The Red Dots show localities where Tsetse Fly was obtained.



MAP SHOWING THE DISTRIBUTION OF SLEEPING SICKNESS IN UGANDA.

The Red Dots show where Sleeping Sickness is prevalent.
The Crosses represent cases imported from Sleeping Sickness area.





into hospital here on August 17, 1904, he had undoubted signs of sleeping sickness, with many trypanosomes in the glands and cerebro-spinal fluid.

The question arises, did this man acquire the disease locally, or was it an imported case? In any case, an individual harbouring so many trypanosomes could readily have infected flies in the belt in which he was working, and so spread the disease. Further information on this point is being obtained.*

Dr. C. A. Wiggins made a journey from Mumia's to Shirati and ascertained the distribution of the fly and sleeping sickness there. In his Report to the P.M.O. East Africa and Uganda Protectorates, dated 30th March, 1904, he mentions a point of considerable interest. He states, "I pitched my tent near Omorie's, close by the river, which runs into Homa Bay, and here I found no tsetse and no sleeping sickness, which surprised me, as I knew sleeping sickness was present on the Lake shore. The country here is open plain, more or less cut off from the Lake by a chain of small circular hills. Afterwards, when interviewing the chief, he told me that he had had sleeping sickness in his villages nearly three years ago, but there was none now, as he had forbidden his people to go to the Lake for fish, or to mix with the Wagemi near the Bay. When I told him that sleeping sickness was caused by the bite of the tsetse, he and all his men readily believed it."

Dr. Wiggins' general conclusions as a result of his observations on the journey are, "(1)—That where there are trees or bushes near the water the flies are found, and sleeping sickness occurs in these places. Conversely, where there are no trees there are no flies and no sleeping sickness; papyrus does not shelter them: also, that there is sleeping sickness inland among those tribes who go to the lake for fish at any point where tsetses are at the Lake shore. (2)—That sleeping sickness spread from Uganda and Usoga eastward and southward. (3)—That there is no sleeping sickness east of a line drawn from the Maragoli hills down the Maragoli stream to the bay, and then across the bay (Kavirondo) to Homa, the three or four cases east of this probably imported. This line is also the eastern limit of the distribution of the tsetse fly with the exception of Kibuye, *i.e.*, Port Florence District. (4)—That the only river which carries the fly inland is the Kuja river, which is the only one that has trees at its mouth and thick vegetation along its course."

The latest information shows that sleeping sickness is occurring on the shores of the Albert Edward Lake.

* *Vide* Report 12 (p. 273).

11. *The Tsetse Flies (Glossina palpalis) which had previously fed on a case of Sleeping Sickness or were freshly caught, can produce in the Monkey an exactly similar disease to that produced by inoculation of fluid containing Trypanosoma gambiense.*

Since the publication of the last Report the after-history of several of the monkeys in whom the infection was produced, either by freshly caught flies at Entebbe, or flies which had previously fed on sleeping sickness cases, has been studied.

The result of these investigations shows that the disease, whether induced by the injection of fluid containing the *Trypanosoma gambiense*, by the bite of the fresh fly or previously infected ones, is, in the monkey, identical in all respects. These facts strongly support the contention that the fresh fly trypanosoma is the *Trypanosoma gambiense*.

A point of interest and importance in this connection is that since the hut tax labourers (one in every two or three of whom had the *Trypanosoma gambiense* in his blood) have left the fly belt at Entebbe, it has taken a very much larger number of flies to infect the monkey than it did when they were present. It is, therefore, fair to assume that the chief source at Entebbe, from which the wild fly obtained its supply of trypanosomes, was the body of men brought in from the various districts for the purpose of hut-tax labour.

EXPERIMENT 97. MONKEY (*Cercopithecus sp.*).

To observe the course of the disease after infection by feeding flies on this monkey eight hours after feeding on a sleeping sickness case.

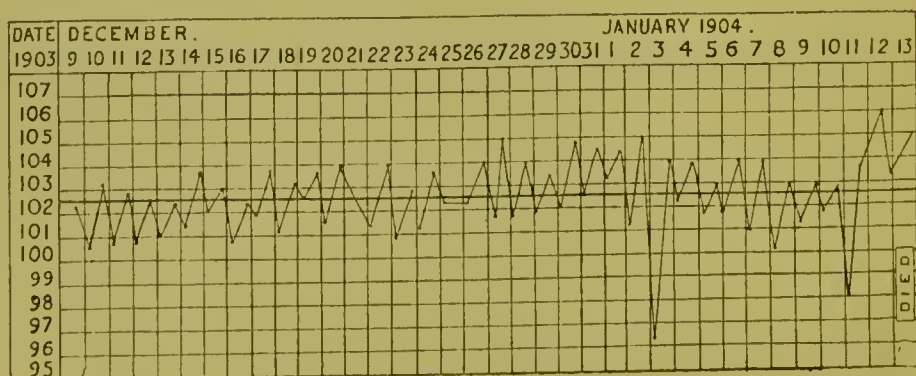
July 1, 1903. Trypanosomes are noted as being in the blood for the first time.

December 18. Animal is beginning to get out of condition.

January 3rd, 1904. Animal has now assumed the characteristic attitude. He is very weak and ill.

January 13. This afternoon he collapsed on the ground, and had convulsive movements of limbs.

The following chart shows the temperature curve:—



The following table shows the presenee or absenee of trypanosomes in the blood and cerebro-spinal fluid.

Date.	Parasites in blood.			Parasites in C.S.F.	
	Filaria.	Malaria.	Tryp.	Tryp.	Strept.
1903.					
July 2	...	+	+
Aug. 3	...	+	—
" 21	...	+	—
Sept. 12	...	+	—
" 25	...	+	—
Oct. 8	...	+	—
Dec. 10	...	+	—
" 13	...	—	—
" 18	...	+	—
1904.					
Jan. 3	...	+	—
" 9	...	+	—
" 13	...	+	+	—	...

January 13. Animal died suddenly at 5 p.m. Post-mortem at once. The body is rather emaciated. Pupils equal and normal. Slight general enlargement of superficial lymphatic glands.

Brain.—On removing the calvarium and reflecting the dura mater some congestion of the superficial vessels is seen. No distinct flattening of convolutions. Cerebro-spinal fluid examined under the microscope, no active trypanosomes seen. Brain removed entire for minute examination. Some increase of fluid in pericardial and peritoneal cavities, no increase of pleural fluid.

Heart.—Nothing noteworthy. Blood from this organ examined on day of death showed the presence of trypanosomes.

Lungs.—Both healthy.

Liver.—Nothing noteworthy.

Spleen.—Slightly enlarged.

Kidneys.—Both healthy.

Glands.—In mesentery and along great vessels are enlarged.

Remarks.—This experiment is of importance as affording proof that the trypanosoma introduced by the bite of flies which had previously fed on a case of sleeping sickness, is capable of inducing in the healthy monkey exactly the same phenomena as those produced by the injection of cerebro-spinal fluid or blood from a sleeping sickness case. The trypanosomes could not be detected in the peripheral circulation on several occasions. They were, however, present on the day of death.

There was no other cause to account for the animal's death apart from the trypanosoma infection. The naked eye changes in the brain were slight.

EXPERIMENT 228. MONKEY (*Cercopithecus sp.*).

To note the effect of the trypanosoma carried by the tsetse flies freshly caught in the vicinity of Entebbe on a monkey.

October 12, 1903. Blood examined. No trypanosomes. Malaria present.

" 13, " Fed 49 flies freshly caught.

" 14, " " 49 "

" 15, " " 24 "

" 16, " " 43 "

" 17, " " 14 "

" 18, " " 18 "

" 19, " " 0 "

" 20, " " 25 "

" 21, " " 12 "

" 22, " " 10 "

" 23, " " 15 "

" 24, " " 32 "

" 25, " " 57 "

" 26, " " 0 "

" 27, " " 32 "

" 28, " " 16 "

" 29, " " 28 "

Blood examined. Trypanosomes absent. Malaria present.

October 30, 1903. Fed 52 flies.

" 31, " " 24 "

November 1, " " 28 "

" 2, " " 0 "

" 3, " " 26 "

" 4, " " 14 "

" 5, " " 30 "

Blood examined. Trypanosomes absent. Malaria present.

November 6, 1903. Fed 20 flies.

" 7, " " 24 "

" 8, " " 17 "

" 9, " " 0 "

" 10, " " 20 "

" 11, " " 18 "

" 12, " " 20 "

Blood examined. Trypanosomes absent. Malaria present.

November 13, 1903. Fed 14 flies.

" 14, " " 26 "

" 15, " " 15 "

" 16, " " 0 "

" 17, " " 28 "

" 18, " " 18 "

" 19, " " 48 "

Blood examined. Trypanosomes absent. Malaria present.

November 20, 1903. Fed 20 flies.

" 21, " " 0 "

" 22, " " 30 "

November 23, 1903. Fed 0 flies.

„ 24, „ „ 20 „

„ 25, „ „ 14 „

„ 26, „ „ 30 „

Blood examined. Trypanosomes *present*. Malaria present.

June 18, 1904. Animal has been distinctly out of condition, and lately has been crouched up. Lumbar puncture at 12.15 p.m.; 2 c.c. cerebro-spinal fluid obtained; this was centrifuged and active trypanosomes obtained.

The temperature from December, 1903, till March, 1904, showed a slight evening rise. From April, 1904, the temperature fell below normal, the morning temperature going as low as 96°.

The following table shows the presence or absence of trypanosomes in the blood:—

Date.				Parasites in the blood.		
				Filaria.	Malaria.	Trypanosoma.
1903.						
Nov.	26	—	+	+
Dec.	3	+	—
„	7	+	+
„	10	+	+
„	17	+	+
„	24	+	
1904.						
Jan.	1	+	+
„	7	+	+
„	14	+	+
„	21	+	—
„	29	+	+
Feb.	4	+	+
„	10	+	+
„	18	+	+
„	25	+	—
March	5	+	+
„	11	+	+
„	18	+	+
„	24	+	+
April	7	+	—
„	14	+	+
„	22	+	+
„	29	+	+
May	6	+	+
„	12	+	+
„	20	+	+
„	27	+	+
June	3	+	+
„	9	+	+
„	16	+	+

June 19. Animal has been lying on the ground to-day in a moribund condition. Killed by chloroform.

The body is markedly emaciated. Skin is rough and coat is staring. No sores. The superficial lymphatic glands in both femoral regions and axillæ are enlarged. The pupils are equal and normal. There is no increase of fluid in the pericardial, pleural or peritoneal cavities.

Heart.—Nothing noteworthy. The blood of this organ contains no active trypanosomes. Stained specimens show the presence of trypanosomes.

Lungs.—Both healthy.

Liver.—Rather mottled appearance.

Spleen.—Enlarged and congested.

Kidneys.—Both rather pale, otherwise healthy.

Brain and Spinal Cord.—Show no noteworthy naked eye change. Both preserved for minute investigation.

Glands.—Abdominal, are slightly enlarged.

Remarks.—This experiment illustrates the course of the disease produced by the trypanosomes carried by the tsetse flies (*Glossina palpalis*) freshly caught in the vicinity of Entebbe. It closely resembles the experiments in which *Trypanosoma gambiense* was injected into the monkey. In both the course of the disease was a prolonged one; the animal in this experiment also showed definite signs for some time before death. At times it presented the same characteristic features met with in the sleeping sickness monkeys. The temperature curve was also very similar. This experiment supports the view that the trypanosoma carried by the freshly caught tsetse flies in Uganda is identical with the *Trypanosoma gambiense*.

EXPERIMENT 301. MONKEY (*Cercopithecus* sp.).

Feeding freshly caught tsetse flies on a healthy monkey.

Blood examination. Trypanosomes absent. Malaria absent.

June 10, 1904. Fed 30 flies.

"	11,	"	"	22	"
"	13,	"	"	30	"
"	14,	"	"	24	"
"	15,	"	"	20	"
"	16,	"	"	27	"
"	17,	"	"	12	"
"	18,	"	"	24	"
"	20,	"	"	14	"
"	21,	"	"	20	"
"	22,	"	"	18	"
"	23,	"	"	15	"
"	24,	"	"	21	"

Blood examination. Trypanosomes absent. Malaria absent.

June 25, 1904. Fed 12 flies.

"	27,	"	"	12	"
"	28,	"	"	20	"
"	29,	"	"	16	"
"	30,	"	"	13	"

	July 1, 1904.	Fed 14 flies.	
	" 2, "	" 22 "	
Blood examination.	Trypanosomes absent.		Malaria absent.
	July 4, 1904.	Fed 23 flies.	
	" 5, "	" 26 "	
	" 6, "	" 19 "	
	" 7, "	" 24 "	
	" 8, "	" 21 "	
	" 9, "	" 25 "	
	" 11, "	" 21 "	
	" 12, "	" 23 "	
	" 13, "	" 20 "	
	" 14, "	" 26 "	
	" 15, "	" 27 "	
	" 16, "	" 12 "	
Blood examination.	Trypanosomes absent.		Malaria absent.
	July 18, 1904.	Fed 32 flies.	
	" 19, "	" 24 "	
	" 20, "	" 40 "	
	" 21, "	" 37 "	
	" 22, "	" 34 "	
Blood examination.	Trypanosomes absent.		Malaria absent.
	July 24, 1904.	Fed 20 flies.	
	" 25, "	" 28 "	
	" 26, "	" 14 "	
	" 27, "	" 18 "	
	" 28, "	" 36 "	
	" 29, "	" 41 "	
	" 30, "	" 30 "	
Blood examination.	Trypanosomes absent.		Malaria absent.
	August 2, 1904.	Fed 37 flies.	
	" 3, "	" 30 "	
	" 4, "	" 16 "	
	" 5, "	" 24 "	
Blood examination.	Trypanosomes absent.		Malaria absent.
	August 8, 1904.	Fed 31 flies.	
	" 9, "	" 32 "	
	" 10, "	" 15 "	
	" 11, "	" 34 "	
	" 12, "	" 12 "	
Blood examination.	Trypanosomes absent.		Malaria absent.
	August 13, 1904.	Fed 27 flies.	
	" 15, "	" 20 "	
	" 16, "	" 14 "	
	" 17, "	" 18 "	
	" 18, "	" 22 "	
	" 19, "	" 16 "	
Blood examination.	Trypanosomes absent.		Malaria absent.
	August 20, 1904.	Fed 37 flies.	
	" 22, "	" 27 "	
	" 23, "	" 24 "	
	" 24, "	" 28 "	

August 25, 1904.		Fed 26 flies.	
„	26, „	„	29 „
Blood examination.		Trypanosomes absent. Malaria absent.	
August 27, 1904.		Fed 21 flies.	
„	28, „	„	30 „
„	29, „	„	24 „
„	30, „	„	16 „
„	31, „	„	14 „
September	1, „	„	30 „
„	2, „	„	26 „
Blood examination.		Trypanosomes absent. Malaria absent.	
September 8, 1904.		Fed 27 flies.	
„	9, „	„	20 „
„	10, „	„	37 „
„	11, „	„	50 „
„	13, „	„	27 „
„	14, „	„	30 „
„	15, „	„	37 „
Blood examination.		Trypanosomes absent. Malaria absent.	
September 16, 1904.		Fed 24 flies.	
„	17, „	„	30 „
„	18, „	„	20 „
„	20, „	„	30 „
„	21, „	„	40 „
„	22, „	„	8 „
„	23, „	„	17 „
Blood examination.		Trypanosomes absent. Malaria absent.	
September 24, 1904.		Fed 24 flies.	
„	25, „	„	32 „
„	27, „	„	12 „
„	28, „	„	26 „
„	29, „	„	30 „
„	30, „	„	14 „
Blood examination.		Trypanosomes absent. Malaria absent.	
October 1, 1904.		Fed 12 flies.	
„	2, „	„	17 „

Animal died. Blood examination. Trypanosomes absent. Malaria absent.

Remarks.—This experiment is of considerable interest, a total of 2,299 flies fed on this monkey yet trypanosomes did not appear in the blood. This indicates that the removal of hut tax labourers from the fly-belt at Entebbe has materially reduced the number of infected flies. Last year when a large number of hut tax labourers were in the belt, about 185 flies were fed on a monkey and produced trypanosomes in the blood.

The animal became very anæmic and debilitated from the loss of blood occasioned daily by the bites and this no doubt caused its death.

12. *Are other varieties of trypanosomes found in Uganda?*

In addition to the *Trypanosoma gambiense*, trypanosomes from various sources have been studied. In the last Report, it was shown that oxen in Entebbe belonging to the P.W.D. and sent for examination by Mr. Pordage, had trypanosomes in their blood. In the blood of government cattle at Jinja, Usoga, which were dying at the rate of five or six a day, a trypanosome was constantly found. In the blood of a dog kindly sent by Mr. R. J. Sturdy, P.V.O. Uganda and East Africa Protectorates, trypanosomes were present. This animal had accompanied the Abyssinian Boundary Commission. Lastly, in the blood of a mule of Col. Sadler's at Entebbe, a trypanosome was found. The trypanosomes derived from these four sources have been studied side by side here.

13. *The History and distribution of these trypanosomes in Uganda and East Africa.*

A. The oxen of Mr. Pordage, as stated in the last Report, came to Entebbe from British East Africa about the end of 1900. They kept well until they were sent to graze in the forest near the Lake, in which *Glossina palpalis* is found. Since then they have been sick, and Mr. Pordage is of opinion that their illness was contracted whilst grazing there.

B. The cattle which became sick and died at Jinja Usoga, and in whose blood a trypanosome was found by us in August, 1903, came from the Bukedi country in May, 1903. They had been in Wamia District to the south-west of Mount Elgon. The route by which they were marched to Jinja Usoga was *via* Igagas, Kibuye, Baleale and Kitindis. They halted at each of these places, and at all of them a species of tsetse fly is found.* To determine whether a trypanosoma occurs in the animals stationed at any of these places, the blood of animals was examined at Kibuye. Mr. Grant kindly made slides from a number of animals in December, 1903. Of ten slides from different domestic animals, trypanosomes were found in two, one in a slide from a donkey, and one from a cow. We were thus able to demonstrate that the necessary factors for the infection of the cattle were present at the halting places.

C. A number of animals which accompanied the Abyssinian Boundary Commission became sick and died, and an examination of one of the sick animals showed that trypanosomes were present in the blood. The animals affected were eleven Boran and Abyssinian ponies, as well as several camels and five English dogs. These all died. None of the Abyssinian donkeys or mules were affected. The English dog examined on August 26th, 1903, was half Airedale and half bull terrier. The animals marched from the boundary to Lake Rudolph, and thence *via* Baringo to Nakuru. Two ponies died at Nakuru. The journey from Baringo to Nakuru only occupies four days,

* *Glossina pallidipes*, see map by Mr. E. E. Austen, Report No. 13.

so that, probably, the infection occurred further north. Austen in his Monograph, p. 326, records that *Glossina fusca* has been found on the north-east shores of Lake Rudolph. *Vide* Map of Distribution of Tsetse Flies in Africa (p. 282).

D. A mule used by Colonel Sadler was found in September, 1903, to have trypanosomes in his blood. This animal had been about five years in Africa, firstly, in the East Africa Protectorate, and for the last eighteen months in Uganda.

14. *Can any difference be made out microscopically between these varieties of trypanosomes occurring amongst the domestic animals in Uganda?*

As the same species of trypanosoma varies in size, shape, etc., in the blood of different experimental animals, too much importance cannot be attached to the morphological characters as affording a means of establishing the identity of different trypanosomes. Speaking generally, it may be safely stated that the trypanosomes found in the blood and cerebro-spinal fluid of cases of sleeping sickness, and in the blood of men showing no signs of sleeping sickness, are always smaller than those of the Jinja cattle, Abyssinian or Entebbe mule disease. The variety met with in the mule showed an unusually large number of short "tadpole" forms. This was especially well seen when the blood containing this variety was injected into a guinea pig (*see* p. 154). The variety met with in the Jinja cattle was, as a rule, larger than the others. It is, however, on morphological grounds only, impossible to arrive at a final conclusion as to the identity or otherwise of the various "strains" brought under our notice. Accordingly, in addition to this means of distinction, their differentiation was approached by a study of their reactions in a series of animals. These reactions were contrasted and compared. Further, the injection of animals proved to be immune to one species with the blood containing another strain of trypanosoma, was used as a means of arriving at a conclusion on the question of the identity or not of the various species. In the drawing of the specimens the morphological characters of the trypanosomes are shown.

15. *Are these trypanosomes pathogenic to animals, and can any difference be made out between them by animal experiment?*

In the case of the trypanosoma found in Mr. Pordage's ox, it produced a very chronic malady in the animals under observation, the animals became extremely emaciated with abnormal temperature. They became gradually weaker and finally died.

The trypanosoma obtained from the Jinja cattle produced few symptoms. There was a general enlargement of the lymphatic glands. As a rule the animals died in fairly good

BLOOD OF DOG SUFFERING FROM
JINGA CATTLE DISEASE.



BLOOD OF DOG.
ABYSSINIAN TRYPANOSOME.



condition. On post-mortem examination the cervical and supra-clavicular lymphatic glands were enlarged and congested. The heart showed yellow jelly-like material at the base, and often petechiæ on its external and internal surfaces. The spleen was slightly enlarged. The native name of the disease is *Sutoko*, and has been considered an internal form of *Mukebi*. The trypanosoma was first found in the herd of cattle in August, 1903. The cattle at the station at Jinja were infected to the extent of 24 per cent. of their number. At Kitindi's, near Jinja, 20 per cent. were infected. Mr. A. G. Boyle, Sub-Commissioner of Usoga, reports "that since March, 1904, the cattle have ceased to die amongst the herd." The herd has been kept at Kitindi's, at which place the *Glossina palpalis* is found. These cattle were again examined in September, 1904. The result of the examination showed that 50 per cent. of these cattle had the trypanosoma in their blood. This examination was made to determine whether the cattle were fit to sell or not. The results show the necessity for such examinations before arriving at a definite opinion on the subject. It is further of interest, as showing that the symptoms of the disease amongst these cattle had undergone considerable modification during the year. In August, 1903, the disease ran a very acute course, the animals dying before any marked signs had developed, whilst in September, 1904, although a larger number of cattle were affected, yet none of them were dying. This fact could be explained in two ways: (1), that the parasite had become attenuated, or (2), the animals had become more immune, or it might be a combination of both factors.

The trypanosoma obtained from the animals which became affected on the Abyssinian boundary caused the death of some eleven Boran and Abyssinian ponies, as well as camels and five English dogs. The Abyssinian donkeys and mules did not suffer. One native (Abyssinian) dog, which was the companion of the English dogs, and had accompanied them on the expedition, remained quite healthy. This animal was, however, susceptible to infection, as was proved by injecting it with blood containing this variety of trypanosoma.

The mule at Entebbe in whose blood a trypanosoma was found, when brought to the laboratory in September, 1903, had slight fever and swelling of the lymphatic glands. A few days later it was brought in a moribund condition. No trypanosomes could be found in the peripheral blood microscopically, but injection of susceptible animals proved the presence of the parasites in the blood.

In the following account of the inoculation of the various experimental animals with the blood of animals suffering from the Jinja cattle disease, Abyssinian fly disease, and the mule disease, the observations are given in full, as this is the first time these diseases have been studied, and it is, therefore, of importance that all the experiments on which conclusions as to the nature of the diseases are based should be given in detail.

In the case of the trypanosoma obtained from Mr. Pordage's ox, it was found impossible to infect either a monkey or a dog with this "strain."

The animals used for inoculation were monkeys, dog-faced baboons, dogs, guinea-pigs, rabbits, donkeys, oxen, sheep, and goats.

A.—*Experiments on the effect on monkeys of the injection of blood containing trypanosomes from animals suffering from "the Jinja cattle disease."*

EXPERIMENT 154. MONKEY (*Cercopithecus* sp.).

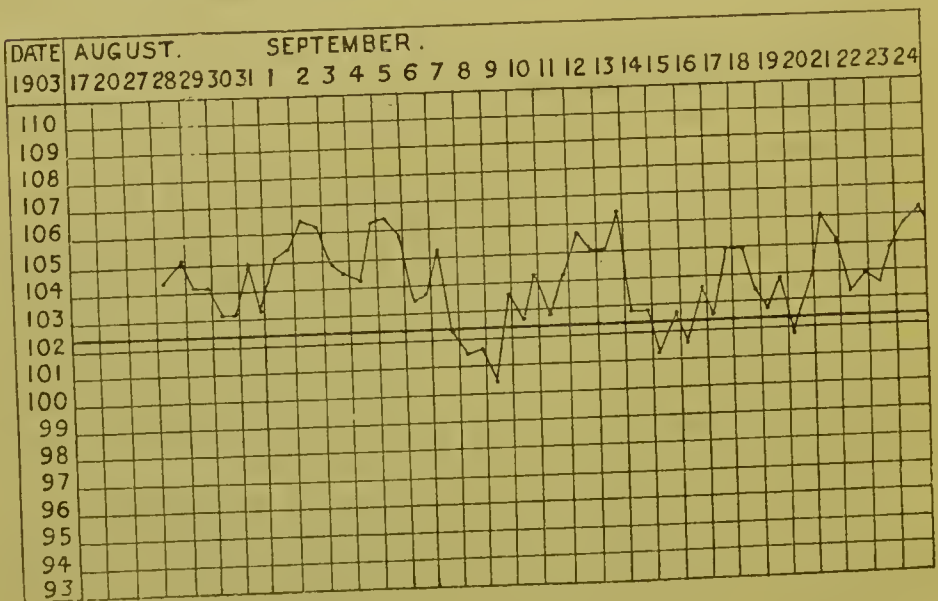
To note the effect of injection of blood from ox suffering from "the Jinja cattle disease" into a monkey.

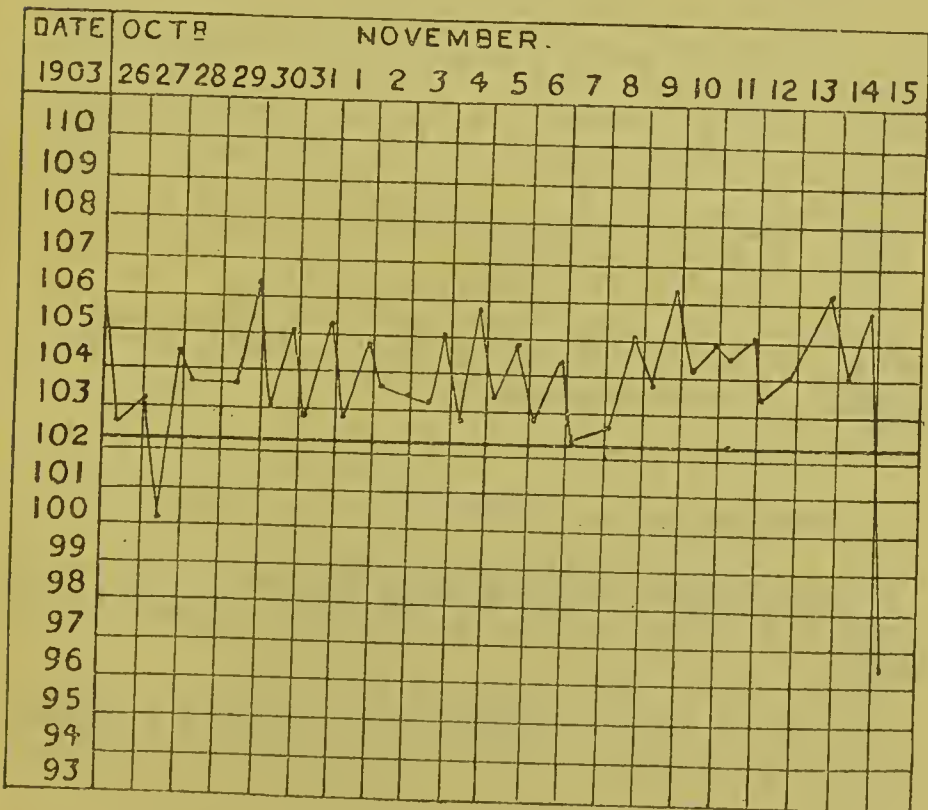
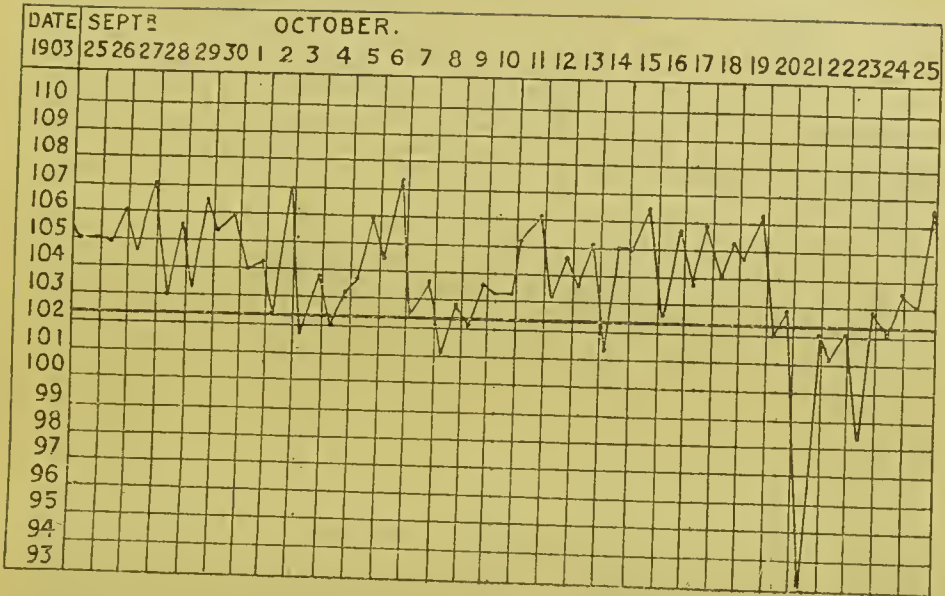
August 17, 1903. Injected subcutaneously 3 c.c. blood containing trypanosomes.

August 27. On examination of the blood trypanosomes were found to be present for the first time; ten days after inoculation.

September 2. Animal is much quieter than usual.

The following chart represents the course of the disease:—





The following table shows the presence or absence of trypanosomes in the blood:—

				Parasites in the blood.		
				Filaria.	Malaria.	Trypanosoma.
Aug.	17	—	+	—
"	20	+	—
"	27	+	+
Sept.	4	+	+
"	6	+
"	12	—	+
"	18	—	+
"	22	+	+
"	25	+	+
"	28	+
Oct.	2	+
"	8	+	+
"	12	+
"	22	—	—
"	25	+
Nov.	4	+
"	12	+

November 15. Animal died at 1.30 p.m. Post-mortem.

The body is emaciated—no enlarged glands or opacity of cornea. There is no increase of fluid in pericardial, pleural or peritoneal cavities.

Heart.—Marked petechiæ on surface—jelly-like substance round base, distinct petechiæ under endocardium of both ventricles.

Lungs.—Both show several small areas of embolism.

Liver.—Nothing noteworthy.

Spleen.—Distinctly enlarged—firm on section.

Kidneys.—Left shows several areas of hæmorrhage on surface and several infarcts on section. Right in similar condition. Glands not enlarged.

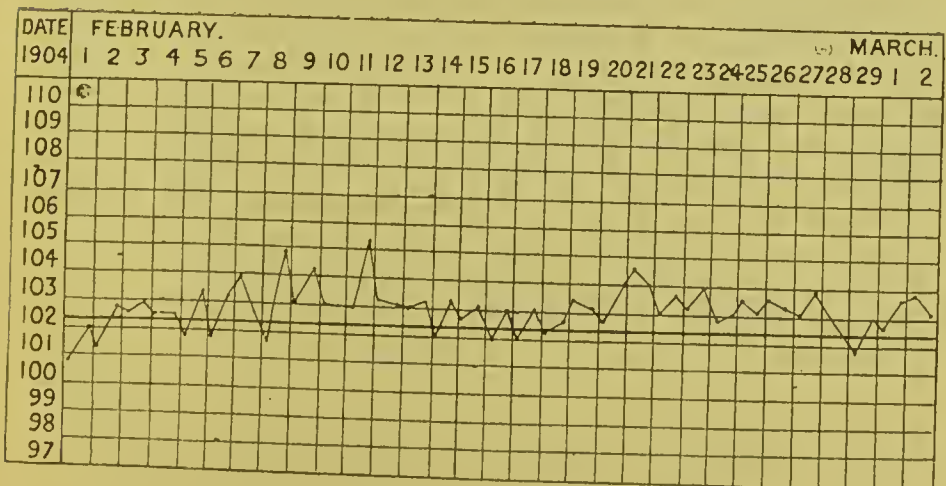
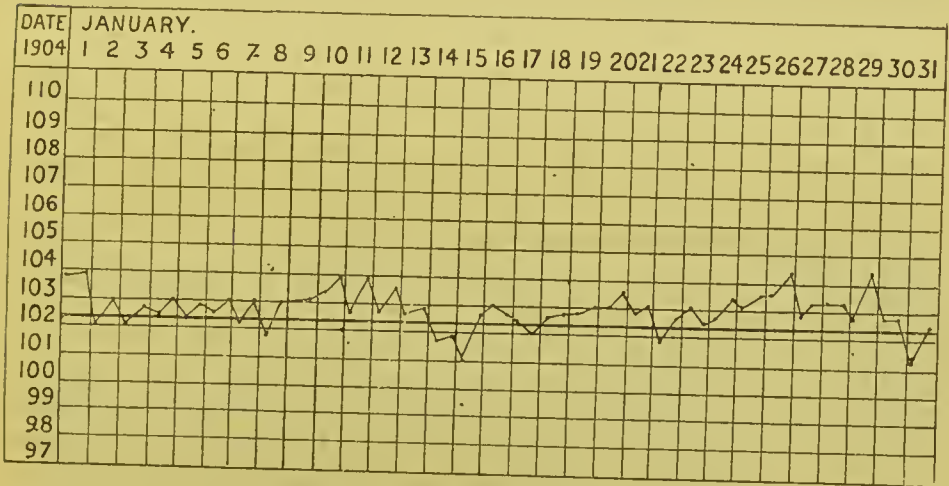
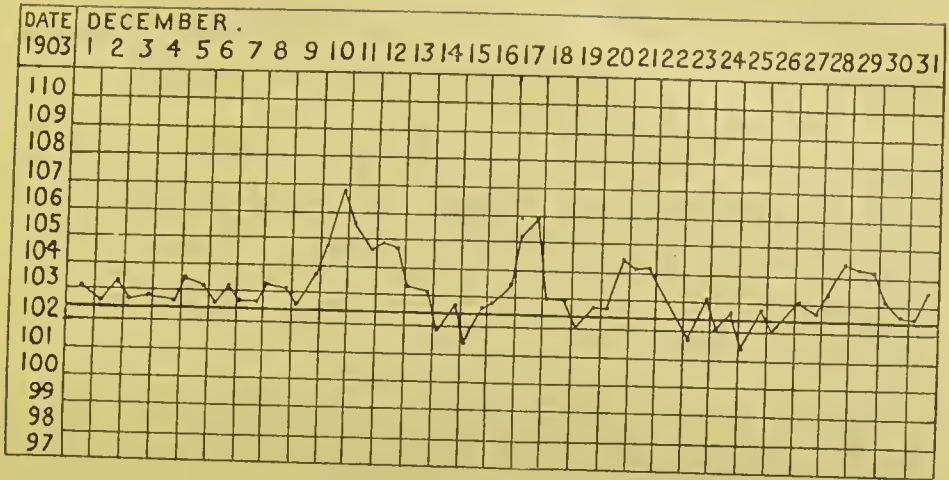
EXPERIMENT 263. MONKEY (*Cercopithecus sp.*).

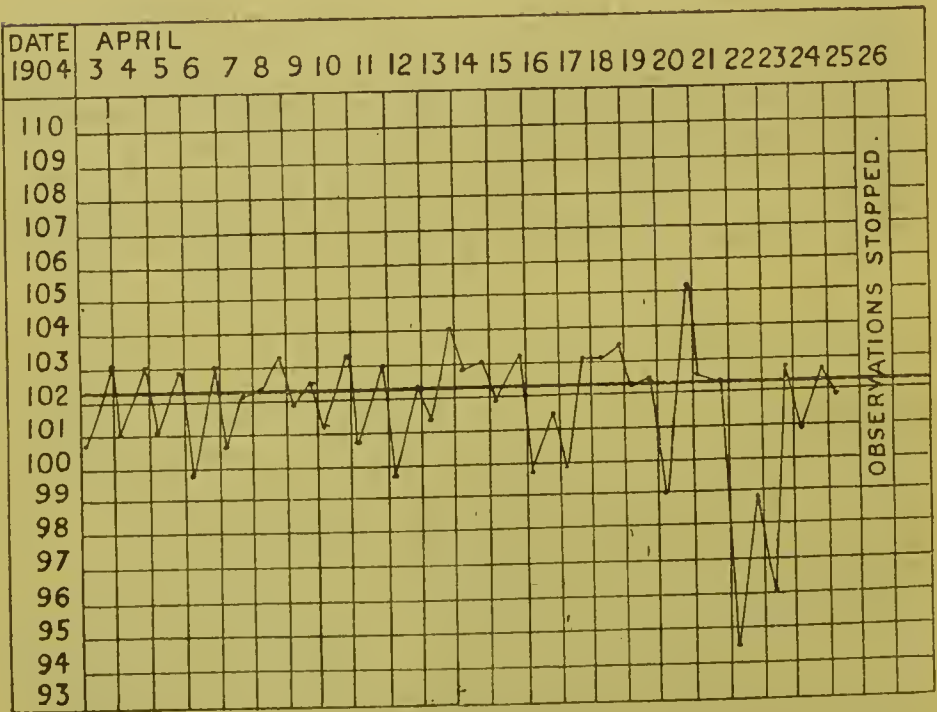
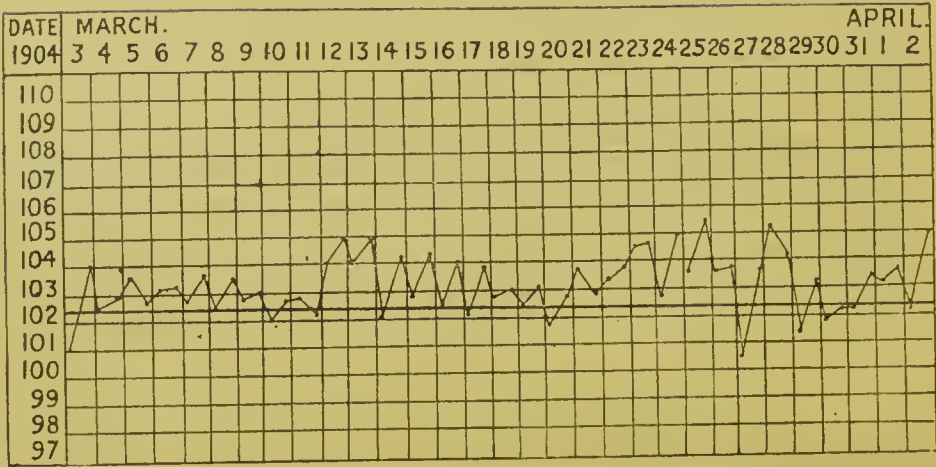
To note the effect of subcutaneous injection of blood from an animal suffering from the "Jinja cattle disease" into a monkey.

December 1, 1903. Injected 5 c.c. of blood containing trypanosomes from the heart of Monkey 241 obtained post-mortem.

December 9. Trypanosomes appeared in the blood to-day, 9 days after injection.

The following chart shows the course of the disease:—





The following table shows the presence or absence of trypanosomes in the blood :—

Date.					Parasites in the blood.		
					Filaria.	Malaria.	Trypanosoma.
1903.							
Dec.	3	—	+	—
"	9	+	+
"	17	+	+
"	24	+	+
"	31	+	+
1904.							
Jan.	7	+	+
"	15	+	+
"	22	+	+
"	28	+	+
Feb.	4	+	+
"	11	+	+
"	18	+	+
"	25	+	—
Mar.	4	+	+
"	18	+	+
"	24	+	+
April	7	+	+
"	14	+	+
"	22	+	—
"	29	+	+
May	6	+	+

May 7. Animal was found dead to-day. He had been partially devoured by a jackal in the night, and many of the organs were removed.

The superficial glands are generally enlarged.

Heart.—No jelly-like substance round base

Remarks.—The long duration of this experiment is of interest and a comparison with Experiment 154 suggests that the longer and more chronic course of the disease in this monkey was, probably, due to alteration of the parasite by passage. About a month before its death only amoebic forms of the parasite were seen in the blood and these were very scanty. Afterwards the trypanosomes increased very rapidly, and swarmed in the blood before death to the extent of 38,000 trypanosomes per c.mm.

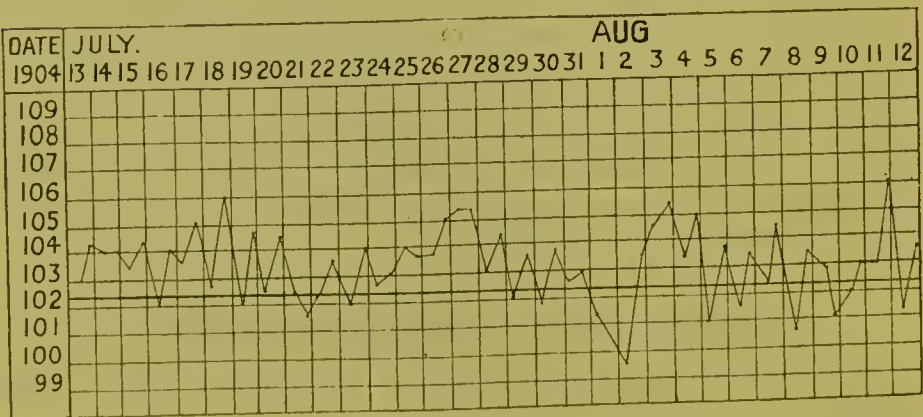
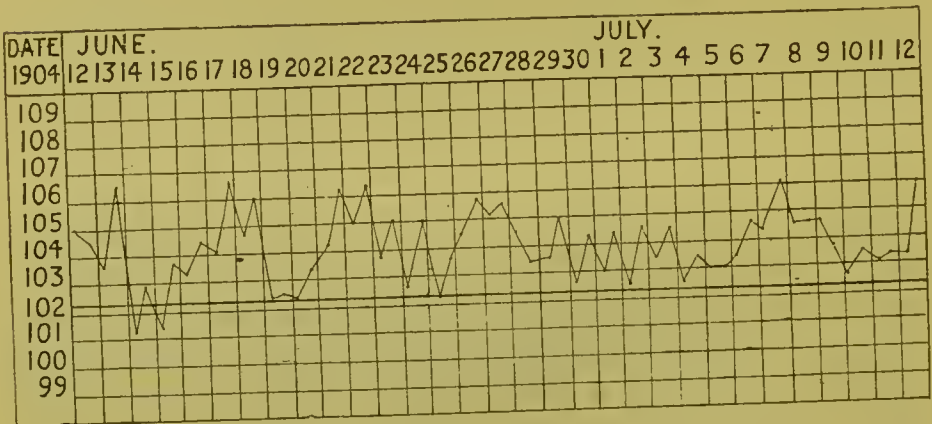
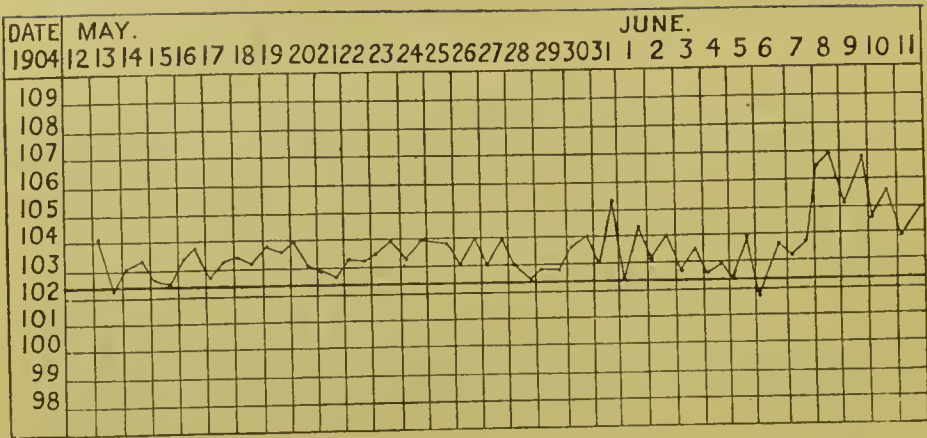
EXPERIMENT 292. WHITE-NOSED MONKEY.

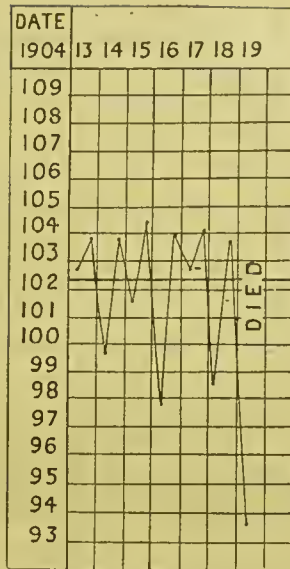
May 12, 1904. Injected 3 c.c. of blood from Monkey 204 (Jinja).

May 31. Injected 1 c.c. blood from dog, Experiment 280.

June 9. Trypanosomes appeared in the blood to-day, 9th day after last inoculation.

The following chart shows the course of the disease :—





The following table shows the presence or absence of trypanosomes in the blood:—

Date.				Parasites in the blood.		
				Fil.	Mal.	Tryp.
1904.						
May 10	—	—	—
" 27	—	—
June 2	—	—
" 9	—	+
" 16	—	+
" 24	—	+
July 2	—	—
" 15	—	+
" 20	—	+
Aug. 5	—	+
" 12	—	+
" 19	—	+

June 19. Animal died at 4 p.m. Post-mortem at once.

The animal is not much emaciated. The coat is out of condition. The superficial glands are generally enlarged.

Heart.—Shows nothing noteworthy. The blood from this organ contains many active trypanosomes and a considerable number of short forms.

Lungs.—Nothing noteworthy.

Liver.—Appears healthy.

Spleen.—Is enlarged and congested—a smear from the pulp shows a number of trypanosomes in various stages of disintegration.

Kidneys.—Show nothing noteworthy.

Lymphatic glands.—In abdomen are enlarged.

Remarks.—This experiment demonstrates the course of this disease in this variety of monkey.

EXPERIMENT 204. MONKEY (*Cercopithecus sp.*).

To observe the effect of the infection produced by flies which fed on this animal after having fed 24 hours previously on an animal infected with the trypanosoma of "Jinja cattle disease."

January 28, 1904. The trypanosomes appeared in the blood to-day for the first time since the feeding commenced.

May 11. Animal has become very thin and out of condition. The coat is staring.

The temperature showed a distinct rise in the evening. Shortly before death it became irregular, swinging between 106° and 97°.

The following table shows the presence or absence of trypanosomes in the blood:—

Date.					Parasites in the blood.		
					Filaria.	Malaria.	Trypanosoma.
1904.							
Feb.	4	+	+
"	11	+	+
"	18	+	—
"	25	+	+
Mar.	4	—	—
"	11	+	+
"	18	+	+
"	24	+	+
April	7	+	+
"	14	+	+
"	22	—	—
"	29	+	+
May	6	+	+
"	12	—	+	+

May 13, 1904. Animal died. Post-mortem.

The body is much emaciated. The lymphatic glands in groin, axillæ and neck are enlarged. Slight increase of fluid in pericardial cavity—no increase of fluid in pleural or peritoneal cavities.

Heart.—Shows nothing noteworthy.

Lungs.—Both healthy.

Liver.—Nothing noteworthy.

Spleen.—Enlarged—firm on section.

Kidneys.—Both healthy.

Intestines.—Large contains some worms, probably trichocephalus.

Great omentum.—*A number of bodies present which look like "maggots," they are covered by a layer of peritoneum and show contractile movements. There were also smaller structures studded throughout the membrane looking like granulation tissue, especially towards the left side near spleen and left kidneys.

The mesentery was also seen to contain similar bodies.

The specimens were preserved for future study.

Remarks.—This experiment clearly showed that the *Glossina palpalis* is capable of transmitting the trypanosoma of the "Jinja cattle disease" after 24 hours. The disease induced by the bite of the fly ran a course which was somewhat more prolonged than in the case of inoculation of blood from diseased cattle into monkeys. This suggests that by passage through monkeys of this species the virulence of this trypanosome has been attenuated.

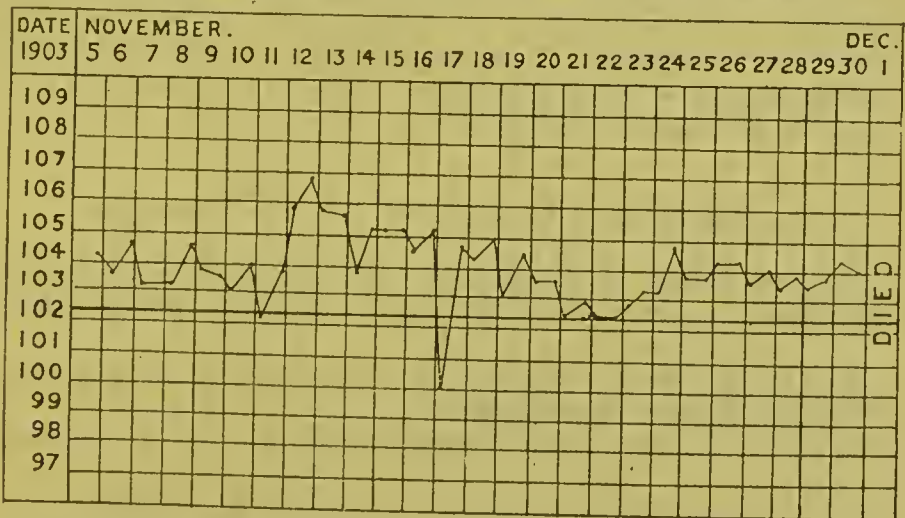
EXPERIMENT 241. MONKEY (*Cercopithecus sp.*).

To note the effect of subcutaneous injection of blood from an animal suffering from the "Jinja cattle disease" into a monkey.

November 9, 1903. Injected 10 c.c. of blood subcutaneously from Dog 234.

November 12. Trypanosomes are present in the blood to-day, 8 days after injection. A filaria was also seen in the blood. It had no sheath; the tail was pointed. Its length was about equal to the *Filaria perstans*.

The following chart shows the course of the disease:—



* Mr. Jeffrey Bell, of the British Museum, on 8th August, 1904, writes "that the parasites are immature examples of *Pentastomum*, several species of which have been found in the peritoneum of monkeys. They would have become mature in the air passages of any carnivora or snake that had eaten the monkey."

The following table shows the presence or absence of filaria and trypanosomes in the blood :—

Date. 1903.	Parasites in the blood.		
	Filaria.	Malaria.	Trypanosoma.
Nov. 5 	—	+	—
„ 12 	+	+	+
„ 14 	+	...	+
„ 19 	+
„ 26 	+
„ 30 	+

December 1, 1903. Animal died. Post-mortem.

No noteworthy external appearance. No increase of fluid in the pericardial, pleural or peritoneal cavities.

Heart.—Shows nothing noteworthy.

Lungs.—Both were distinctly œdematous and showed patchy areas of congestion.

Liver.—Was distinctly fatty.

Spleen.—Was somewhat enlarged and showed small areas like sago grains.

Kidneys.—Nothing noteworthy.

The connective tissue of peritoneum was carefully examined but no trace of a parent filaria could be found there or in the pelvis. Other situations were also examined with negative results.

Brain.—Showed nothing noteworthy.

Remarks.—The course of the trypanosoma infection was probably shortened by the morbid condition found in the lungs and liver. The finding of a filaria in this monkey was of considerable interest. It is the first time a filaria has been found in any of the monkeys here. It does not seem to belong to any of the known varieties.

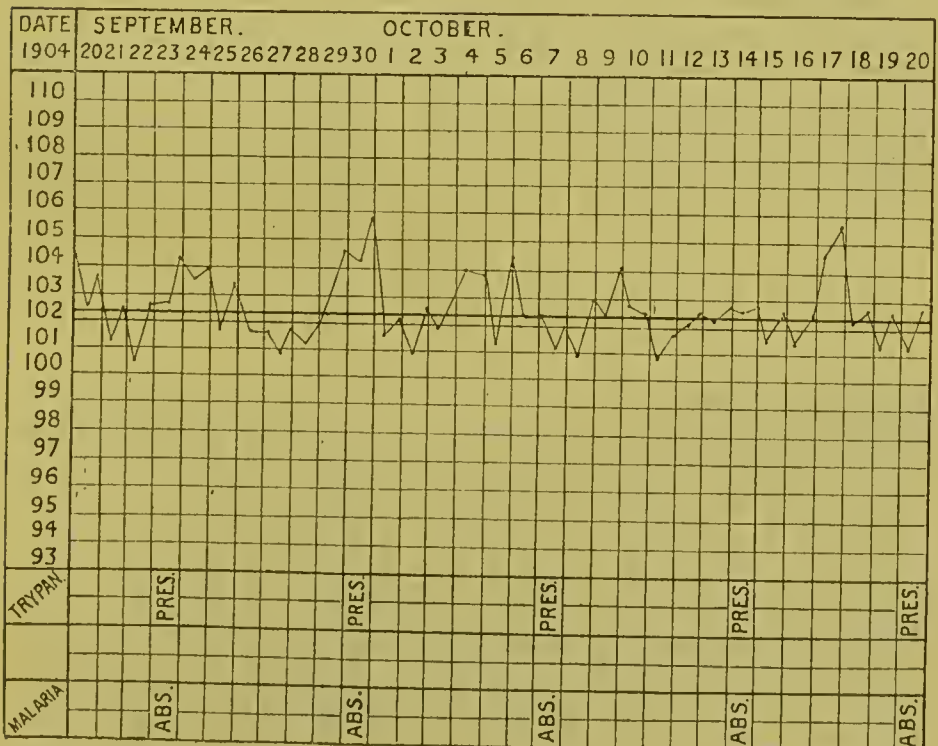
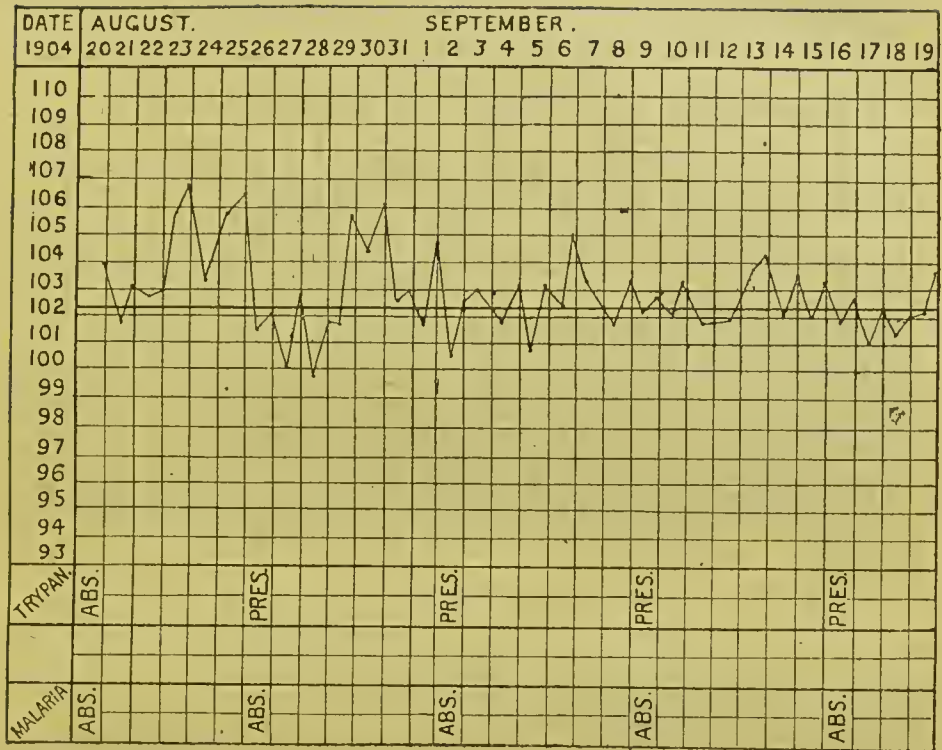
EXPERIMENT 315. MONKEY (*Cercopithecus* sp.).

To note effect of subcutaneous injection of blood from an animal suffering from the “Jinja cattle disease” into a monkey.

August 19, 1904. Injected 2 c.c. of blood containing many trypanosomes from Monkey 292.

October 2. General condition shows no noteworthy change.

The following chart shows the course of the disease :—



B. *Experiments on the effect on monkeys of the injection of blood containing trypanosomes from animals suffering from the "Abyssinian fly disease."*

EXPERIMENT 134. MONKEY, WHITE-NOSED (*sp.?*).

To note the effect of blood containing trypanosomes from an animal sent from Abyssinia with a monkey.

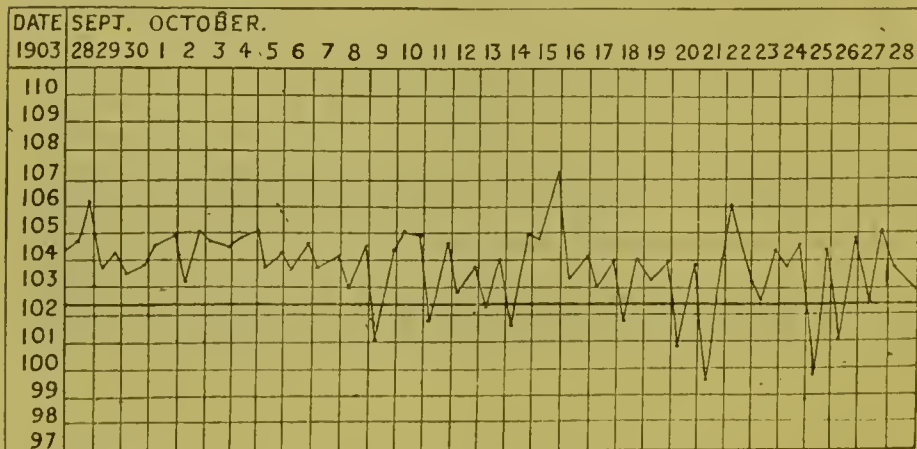
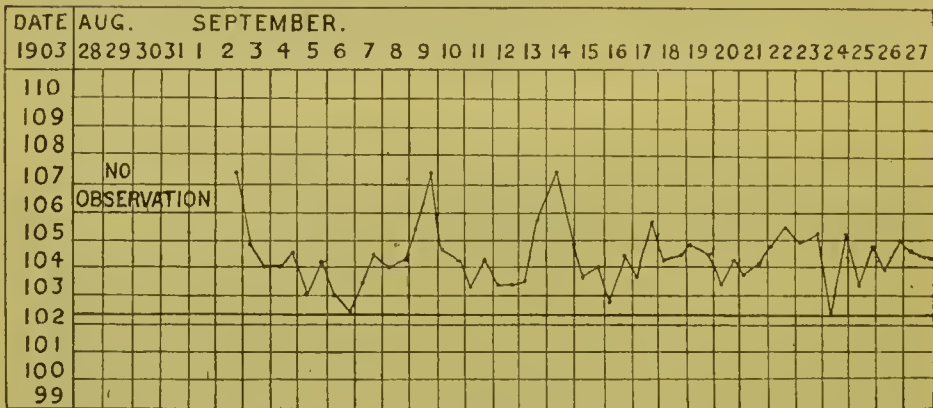
August 28, 1903. 3 c.c. of blood from dog, Experiment 160, subcutaneously.

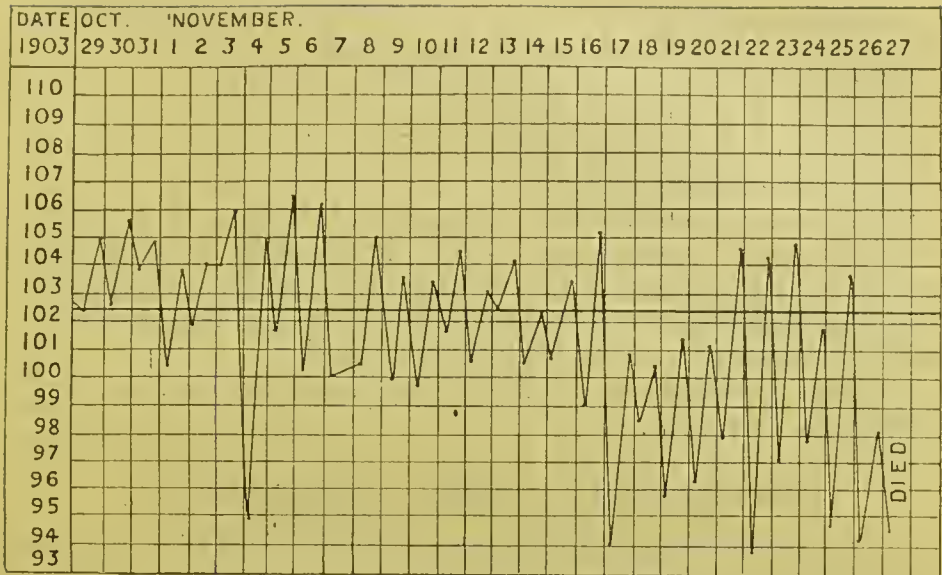
September 2. The blood was examined and trypanosomes were found to be present five days after inoculation.

November 7. The animal is getting thin and shows a tendency to lie about. The breathing is rapid.

November 25. This is now very sick and unable to rise.

The following chart represents the temperature curve:—





The following table shows the presenee or absenee of trypanosomes in the blood :—

Date. 1903.				Parasites in the blood.		
				Filaria.	Malaria.	Trypanosoma.
Aug. 21	—	+	—
" 28	+	—
Sept. 2	+
" 3	+
" 4	+
" 5	—
" 12	—	+
" 18	+	—
" 22	—
" 25	+	+
" 28	+	+
Oct. 5	+
" 12	—	—
" 15	+
" 18	—
" 22	—	+
" 29	+
Nov. 5	+
" 6	—	—
" 12	+
" 17	+
" 25	+

November 27. Animal died. Post-mortem.

The animal is markedly emaciated; no opaeity of cornea, glands not enlarged.

On opening the body there is no inerease of fluid in the pericardial, pleural or peritoneal eavities.

Heart.—A few petechiæ under epicardium of left ventricle. Fat at base is absorbed, otherwise normal.

Lungs.—Both show areas of minute ecchymosis.

Liver.—Nothing noteworthy.

Kidneys.—Left shows 2 areas of infarction quite colourless.

Spleen.—Not enlarged.

Glands.—Glands in the mesentery enlarged and congested.

Brain and Spinal Cord.—The dura mater was markedly adherent to the calvarium. No increase of subarachnoid fluid. The convolutions were slightly congested. The brain and spinal cord preserved for minute examination.

Remarks.—This experiment represents the course of the disease in a monkey.

EXPERIMENT 224. MONKEY (*Cercopithecus* sp.).

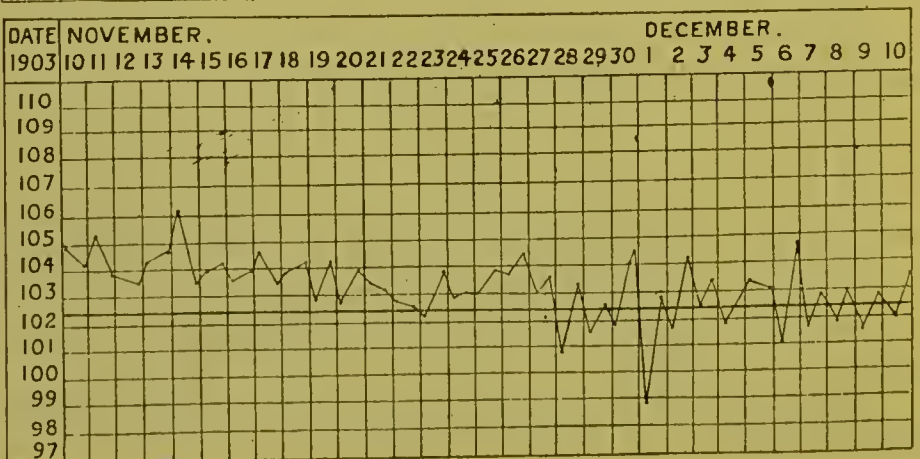
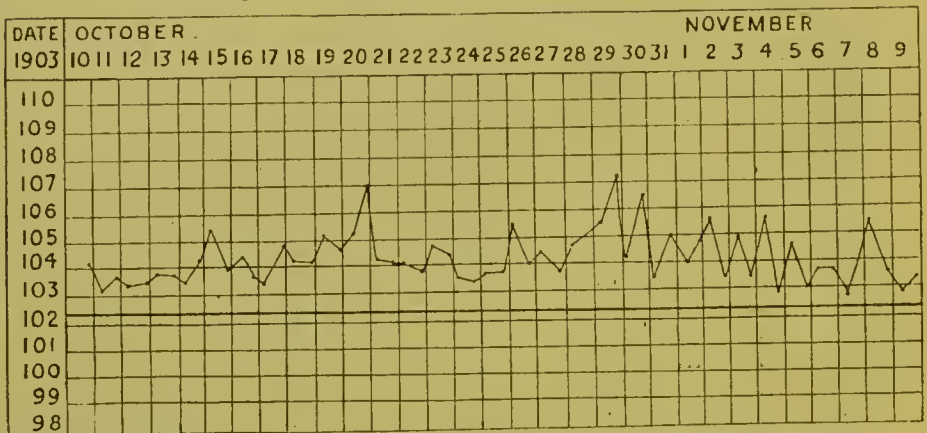
To note the effect of subcutaneous injection of blood from an animal suffering from the "Abyssinian fly disease" into a monkey.

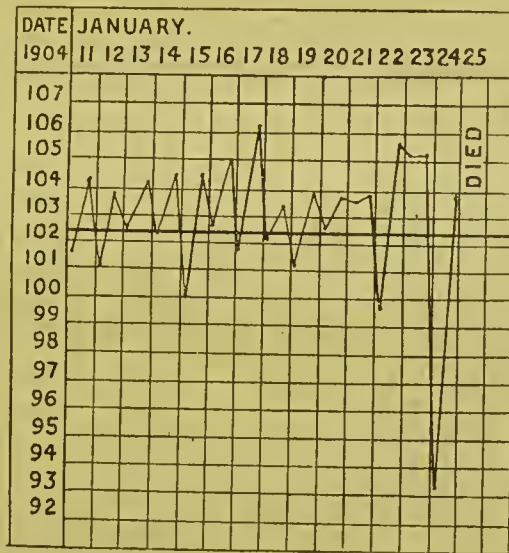
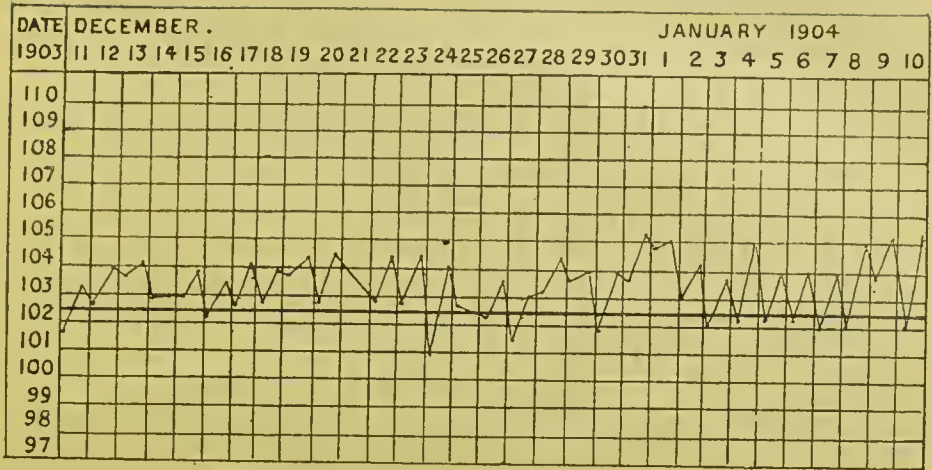
October 10, 1903. Injected 5 c.c. blood from Dog 177 taken post-mortem containing active trypanosomes.

November 16. Re-injected with a few drops of blood from Dog 243 containing active trypanosomes.

January 24, 1904. Animal is very sick. The face is distinctly swollen.

The following chart shows the course of the disease:—





The following table shows the presence or absence of trypanosomes in the blood:—

Date.		Parasites in the blood.		
		Filaria.	Malaria.	Trypanosoma.
1903.				
Oct.	12
"	16
"	22
"	26
"	29
Nov.	2
"	5
"	12
"	19
"	21
"	25
"	26

Date.					Parasites in the blood.		
					Filaria.	Malaria.	Trypanosoma.
1903.							
Dec.	3	+	+
"	10	+	-
"	17	+	+
"	24	+	-
"	31	+	+
1904.							
Jan.	1	+	+
"	7	+	+
"	14	+	+
"	21	+	+

January 25. Animal died in the night. Post-mortem.

An œdematous swelling on right side of muzzle. The pupils are equal and normal. The superficial glands are slightly enlarged. No emaciation.

Some increase of fluid in pericardial cavity, no increase of fluid in pleural or peritoneal cavities.

Heart.—Appears healthy. Trypanosomes present in the blood of this organ.

Lungs.—Both healthy.

Brain and Spinal Cord.—No naked eye change. Preserved for minute investigation.

Glands.—Abdominal slightly enlarged.

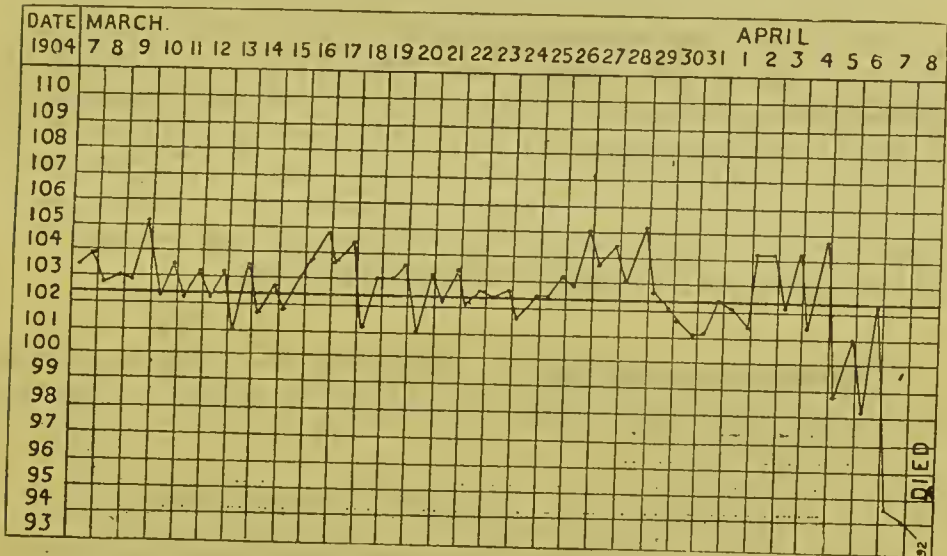
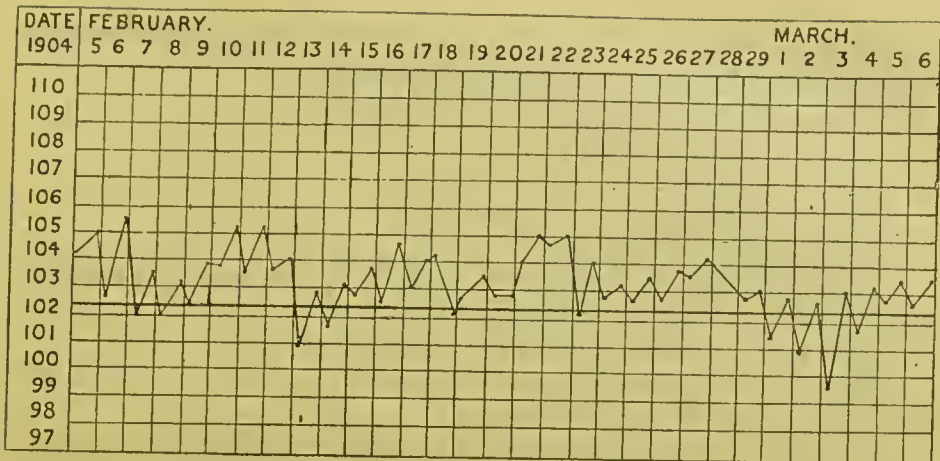
Remarks.—This animal died in comparatively good condition. The experiment illustrates the course of the disease produced by this variety of trypanosomes in a monkey.

EXPERIMENT 252. MONKEY (*Cercopithecus sp.*).

To observe the effects of the infection produced by tsetse flies (*Glossina palpalis*) which fed on this animal after having fed 24 hours previously on an animal infected with the trypanosoma of the "Abyssinian fly disease."

February 4, 1904. The trypanosomes appeared in the blood to-day for the first time since the feeding commenced.

The following chart shows the course of the disease :—



The following table shows the presence or absence of trypanosomes in the blood:—

Date.	Parasites in the blood.		
	Filaria.	Malaria.	Trypanosoma.
1904.			
Feb. 11
" 18
" 25
Mch. 4
" 11
" 18
" 24
April 7

April 9. Animal dying. Killed by chloroform.
A slight general enlargement of superficial lymphatic glands. There is no increase of pericardial or pleural fluid.

Brain and Spinal Cord.—No noteworthy change naked eye. Preserved entire for minute investigation.

Heart.—Shows no noteworthy change.

Lungs.—Both healthy.

Liver.—Healthy.

Spleen.—Enlarged and congested

Kidneys.—Both healthy.

Intestine.—An exudation of thick lymph is seen surrounding the rectum, which is adherent to the vagina. The rectum shows a small perforation at its upper part.

Glands.—A drop of juice examined microscopically shows actively motile trypanosomes.

Remarks.—This experiment had already fulfilled its primary object, viz., to ascertain whether *Glossina palpalis* conveyed the trypanosoma of the "Abyssinian Fly Disease" after an interval of 24 hours, and it showed that it could do so. This is of importance both from the fact that this variety of trypanosome is capable of transmission by the *Glossina palpalis* and also that *Glossina palpalis* is able to convey not only the Trypanosoma gambiense, but other varieties of trypanosomes. The perforation of the rectum, which was caused by the passage of a thermometer, undoubtedly hastened the death.

C. *Experiments on the effect on Monkeys of the injection of blood containing Trypanosomes from animals suffering from the "Mule Disease."*

EXPERIMENT 180. MONKEY (*Cercopithecus* sp.).

To note the effects of subcutaneous injection of blood from an animal suffering from the "Mule disease" into a monkey.

September 13, 1903. Injected subcutaneously 20 c.c. blood from Col. Saddler's mule. No trypanosomes could be found even after centrifuging the blood.

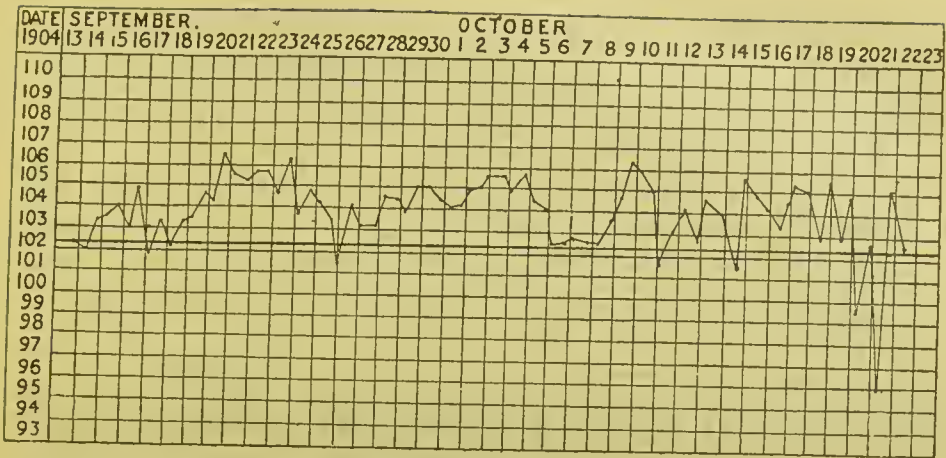
September 20. Trypanosomes appeared in the animal's blood to-day, 7 days after injection.

September 25. The trypanosomes had a peculiar appearance, being crescentic in shape, with a broad thick body and short flagellum. The protoplasm is very vacuolated.

September 28. Some blood removed by opening femoral artery to inject other animals.

October 20. The animal is very sick to-day and is unable to rise. The femoral artery was opened and 5 c.c. blood taken to inject other animals.

The following chart represents the course of the disease:—



The following table shows the presence or absence of trypanosomes in the blood:—

Date.					Parasites in the blood.		
					Filaria.	Malaria.	Trypanosoma.
1903.							
Sept.	14	-	-	-
"	18	-	-
"	20	-	+
"	22	-	+
"	25	-	+
"	26	-	+
"	28	-	+
Oct.	2	-	+
"	3	-	+
"	4	-	+
"	8	-	+
"	10	-	+
"	13	-	+
"	19	-	+
"	20	-	+
"	22	-	+

October 23. Animal died. Post-mortem.

The body is considerably emaciated. No enlarged glands. No oedematous swellings.

There is some increase of fluid in the pericardial cavity, no increase of fluid in pleural or peritoneal.

Heart.—Nothing noteworthy.

Lungs.—Show slight congestion.

Liver.—Has mottled appearance.

Spleen.—Somewhat enlarged. Examination of the pulp shows trypanosomes, which are considerably modified in appearance.

Kidneys.—Appear healthy.

Brain.—Was removed entire for further investigation.

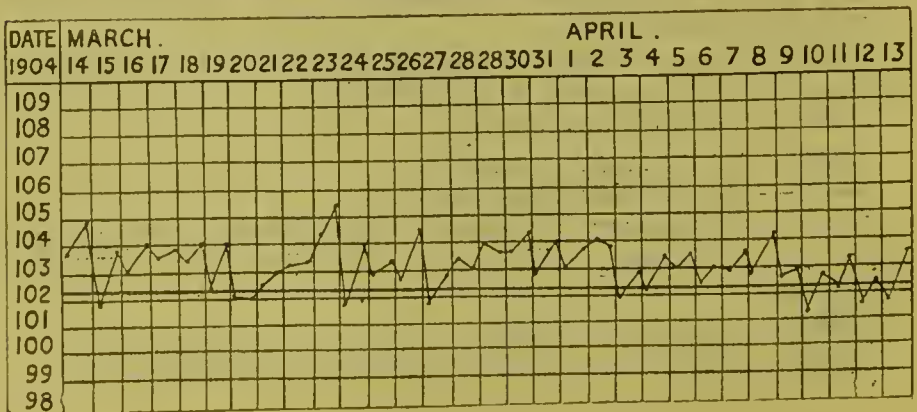
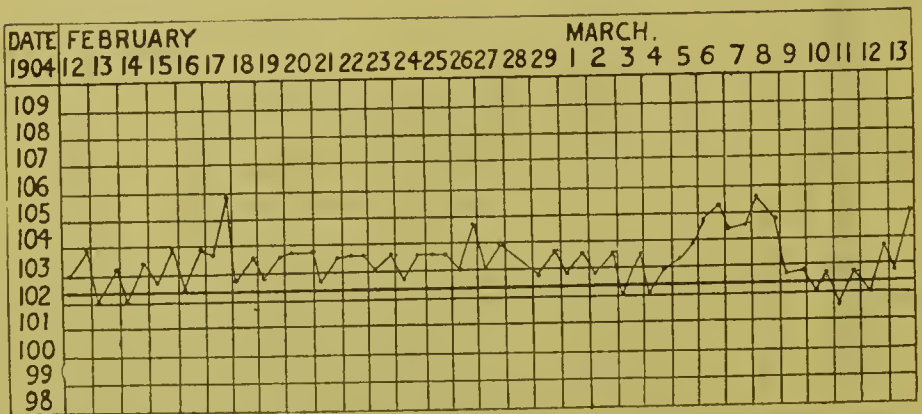
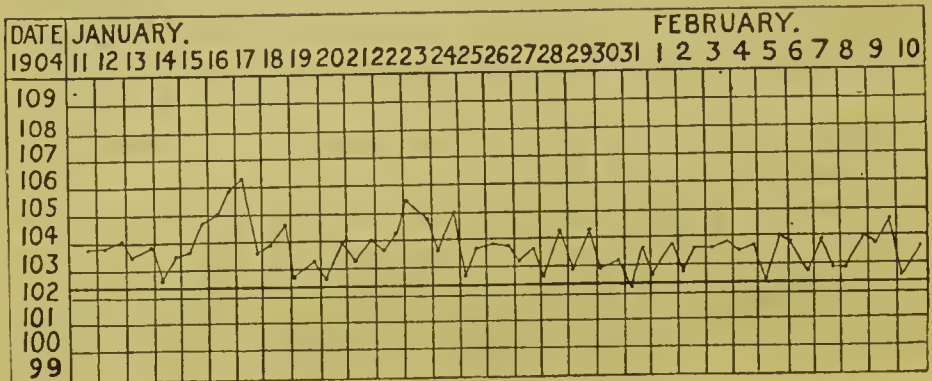
EXPERIMENT 276. MONKEY (*Cercopithecus sp.*).

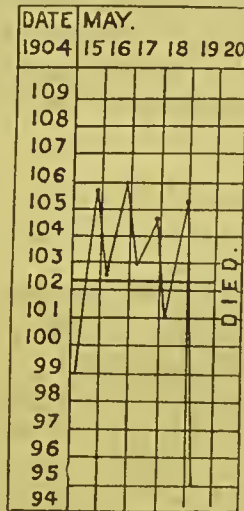
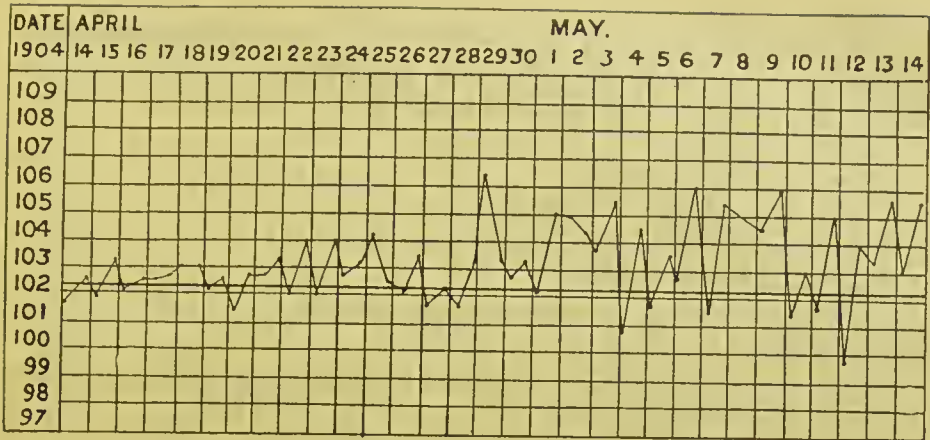
To note the effect of subcutaneous injection of blood from an animal suffering from the "Mule disease" into a monkey.

January 11, 1904. Injected 0.75 c.c. of blood subcutaneously from guinea-pig, Experiment No. 182.

May 11. Animal has been getting very thin and out of condition.

The following chart shows the course of the disease:—





The following table shows the presence or absence of trypanosomes in the blood :—

Date.				Parasites in the blood.		
				Filaria.	Malaria.	Trypanosoma.
1904.						
Jan.	15	—	+	+
"	20	+	+
"	28	+	+
Feb.	4	+	+
"	18	+	+
"	25	+	+
March	4	+	+
"	11	+	+
"	18	—	+
"	24	—	+
April	7	+	+
"	14	—	+
"	22	+	+
"	29	+	+
May	6	+	+
"	12	+	+
"	20	+	+

May 20. Animal died. Post-mortem.

The body is markedly emaciated. General enlargement of superficial lymphatic glands. No increase of fluid in the pericardial, pleural or peritoneal cavities.

Heart.—Normal.

Lungs.—Both healthy.

Liver.—Nothing noteworthy.

Spleen.—Enlarged and firm on section.

Kidneys.—Both healthy.

Intestines.—Some recent lymph round the rectum and hepatic flexure of colon.

Lymphatic Glands.—In omentum and along great vessels are distinctly enlarged.

Brain.—Naked eye shows no noteworthy change.

Remarks.—This experiment shows the course of this disease in a monkey. Possibly the local peritonitis, caused by damage to rectum by thermometer, helped the fatal issue.

Experiments on the effect of the injection of these Trypanosomes into Dogs.

The native dog of Uganda, on account of the frequency with which anchylostomiasis occurs amongst them, is not suitable as an experimental animal.

However, it was possible to determine that the dog is susceptible to all these "strains" of trypanosomes. The disease caused by them in dogs is invariably fatal. Amongst the signs met with during life are opacity of the cornea, emaciation, anæmia and fever. Oedematous swellings were not present. The lymphatic glands were occasionally enlarged, but not markedly so.

Injection of blood containing Trypanosomes from animals suffering from the "Jinja Cattle Disease" into Dogs.

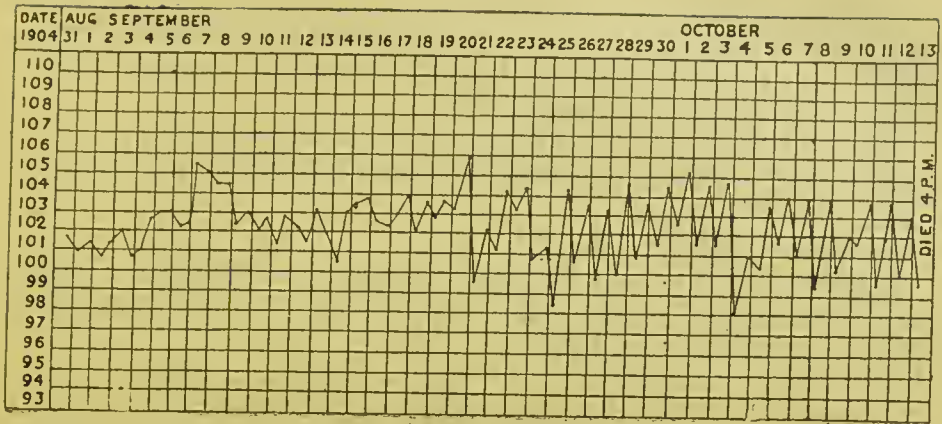
EXPERIMENT 164. DOG.

August 31, 1903. Injected 0.5 c.c. blood subcutaneously from Monkey 135, in whose blood the trypanosoma of the "Jinja cattle disease" was present.

September 13. The animal is noticed to be getting thin.

October 2. The animal is now very emaciated. The blood is pale and watery.

The following chart represents the course of the disease :—



The following table shows the presence or absence of trypanosomes in the blood:—

Date.				Parasites in the blood.		
				Filaria.	Malaria.	Trypanosoma.
1903.						
August	31	—	...	—
Sept.	3	—	...	—
"	5	+
"	6	+
"	7	+
"	8	+
"	9	+
"	12	+
"	14	+
"	16	+
"	17	+
"	21	+
"	23	+
"	26	+
"	29	+
October	2	+
"	5	+
"	9	+
"	10	+
"	13	+

October 13. Animal died at 4 p.m. Post-mortem.

There is marked emaciation. A slight opacity of right cornea. No œdema present. No increase of fluid in the pleural, pericardial or peritoneal cavities.

Heart.—Many petechiæ and ecchymoses on the anterior surface of the right ventricle. None observed under endocardium.

Lungs.—Both show numerous embolic areas. The microscopic examination of these areas shows trypanosomes variously altered from the typical appearance. Some are circular with a larger and smaller chromatin dot.

Liver.—Has a mottled appearance, probably fatty.

Spleen.—Is distinctly enlarged, measuring 10 in. \times 3 in. On section it is fairly firm.

Kidneys.—Both are healthy.

Lymphatic glands.—A few are enlarged and congested in the posterior triangle of neck, also in the mesentery; these on section are seen to be hæmorrhagic.

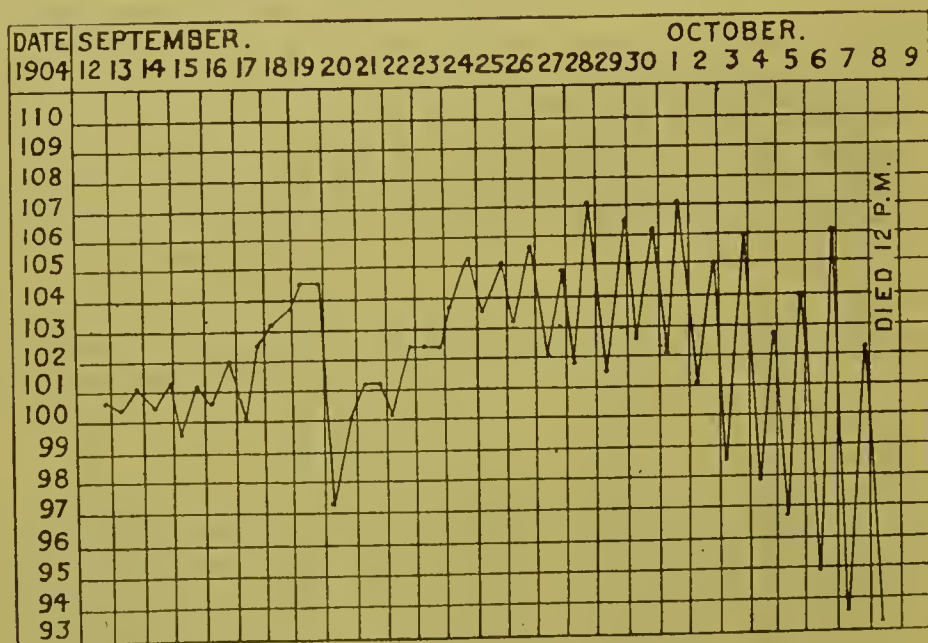
EXPERIMENT 178. DOG.

To note the effect of subcutaneous injection of blood from an animal suffering from the "Jinja cattle disease" into a dog.

September 12, 1903. Injected subcutaneously 0.5 c.c. blood containing trypanosomes from Experiment 164.

October 8. The animal has got thinner lately and is becoming markedly anæmic.

The following chart shows the course of the disease:—



The following table shows the percentage of hæmoglobin and the presence or absence of trypanosomes:—

Date.				Hæmo- globin.	Parasites in the blood.		
					Filaria.	Malaria.	Tryp.
1903.				Per cent.			
Sept.	12	—	—	—
"	15	—	—	—
"	17	—	—	+
"	21	78	—	—	+
"	23	60	—	—	+
"	26	50	—	—	+
"	29	35	—	—	—
October	2	28	—	—	—
"	5	18	—	—	—
"	8	—	—	+

October 8. Animal died at 12.30 p.m. Post-mortem at once.

The body is emaciated. No enlarged superficial glands or oedema. No increase of fluid in the pleural, pericardial or peritoneal cavities.

Heart.—Muscle is pale, no petechiæ. The blood of this organ contains active trypanosomes.

Lungs.—Nothing noteworthy.

Liver.—Apparently healthy.

Spleen.—Is enlarged about 9 inches \times 2 inches.

Kidneys.—Both very pale.

Stomach.—Shows *Spiroptera sanguinolenta* in the wall.

Intestines.—Contain ankylostomes and tapeworm.

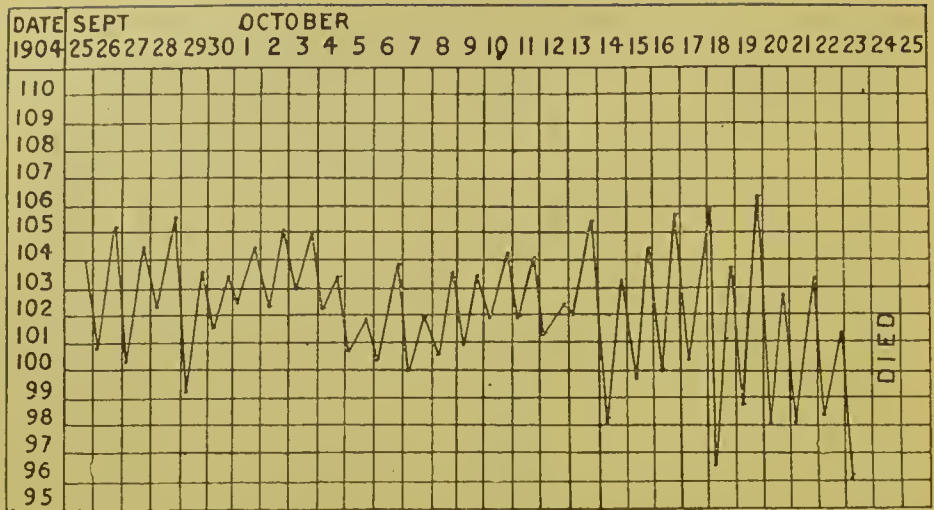
Remarks.—The fatal termination of this experiment was undoubtedly due to the ankylostomiasis.

EXPERIMENT 200. DOG.

To note the effect of subcutaneous injection of blood from animal suffering from the "Jinja cattle disease" into a dog.

September 25, 1903. Injected subcutaneously 4 c.c. blood from Monkey 135, containing active trypanosomes.

The following chart shows the course of the disease :—



The following table shows the presence or absence of trypanosomes in the blood :—

Date.					Parasites in the blood.		
					Filaria.	Malaria.	Trypanosoma.
1903.							
Sept.	26	—	—	—
"	29	—
Oct.	2	+
"	5	+
"	8	+
"	12	+
"	15	+
"	19	+
"	24	+

October 24. Died. Post-mortem.

The body is emaciated. There is no opacity of corneæ. Some increase of fluid in pericardial cavity seen, no increase of fluid in pleural or peritoneal cavities.

Heart.—Shows many petechiæ under epicardium of the left ventricle. Also petechiæ under endocardium of each ventricle. The blood of this organ contained active trypanosomes.

Lungs.—Very congested, the right shows many embolic areas. Examined microscopically these areas are seen to contain some enlarged and vacuolated trypanosomes, and many are unaltered.

Liver.—Normal.

Spleen.—Enlarged, measures 8 inches × 2 inches. On the surface towards its posterior end are two tumours, about the size

of a bean. The interior is distinctly congested and they are apparently encapsuled. Films were made and showed trypanosomes of normal appearance. On section of spleen a similar tumour was seen not protruding beyond the surface.

Kidneys.—Pale, otherwise nothing noteworthy.

Intestines.—Contain tape-worms and anchylostomes.

Glands.—Retroperitoneal are enlarged.

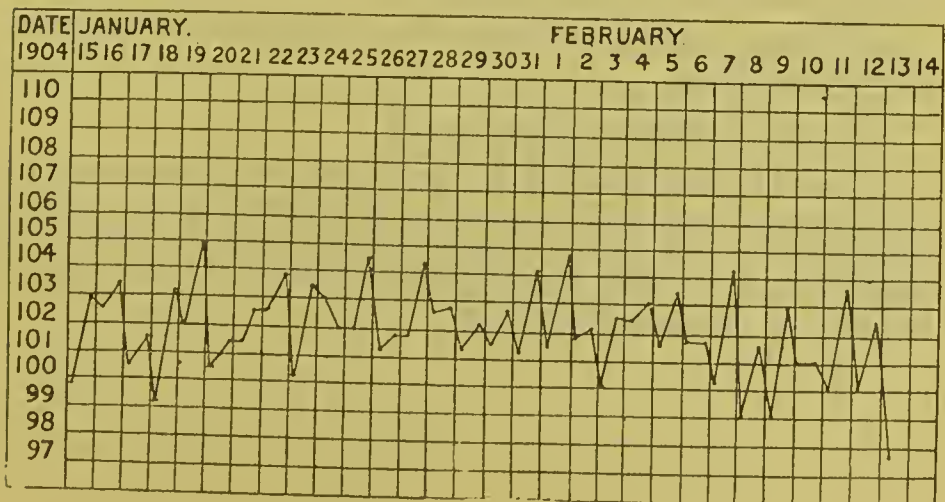
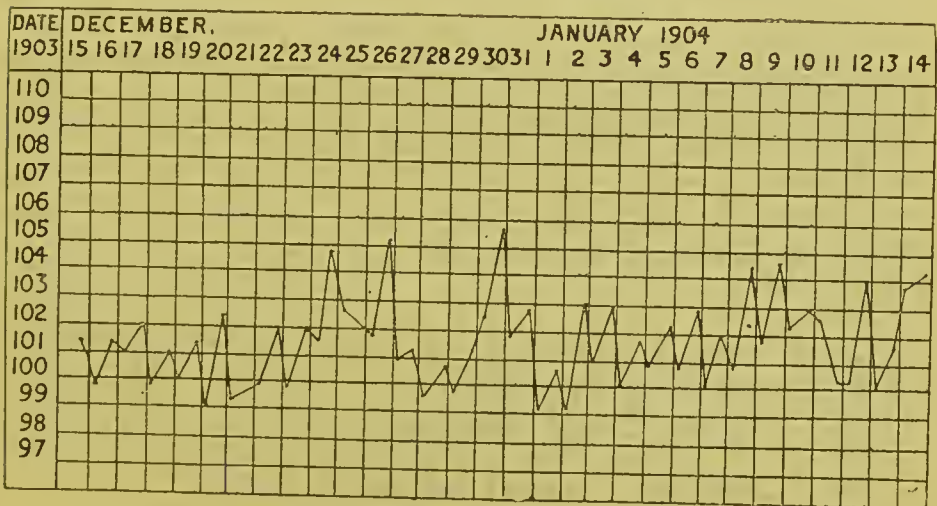
EXPERIMENT 269. DOG.

To note the effect of subcutaneous injection of blood from an animal suffering from the "Jinja cattle disease" into a dog.

December 15, 1903. Injected subcutaneously 8 c.c. of blood from goat, Experiment 192.

February 2, 1904. Animal has now got well-marked corneal opacity in both eyes.

The following chart shows the course of the disease:—



The following table shows the presence or absence of trypanosomes in the blood:—

Date.					Parasites in the blood.		
					Filaria.	Malaria.	Trypanosoma.
1903.							
Dec.	21	—	—	—
"	26	+
"	29	+
1904.							
Jan.	6	+
"	12	+
"	19	+
"	26	+
Feb.	2	+
"	9	+

February 15. Animal died last night. Post-mortem.

The body is markedly emaciated and both corneæ are quite opaque. The glands are not enlarged.

No increase of fluid in the pericardial, pleural or peritoneal cavities.

Heart.—No petechiæ, a jelly-like material round base. The blood from this organ shows a number of altered trypanosomes.

Lungs.—The right shows a few areas of hæmorrhage, the left shows nothing noteworthy.

Liver.—No noteworthy change.

Spleen.—Slightly enlarged and soft on section.

Kidneys.—Nothing noteworthy.

Intestines.—A few anchylostamata are present in upper part of small intestine.

Lymphatic glands.—Not enlarged.

Remarks.—The blood of the goat with which the animal was injected did not show trypanosomes in films at the time of injection, but still proved capable of infecting the dog. The general course of the disease presented the usual characters of the disease as met with in dogs.

B. *Injection of blood containing Trypanosomes from animals suffering from the Abyssinian Fly Disease into Dogs.*

EXPERIMENT 160. DOG, LARGE.

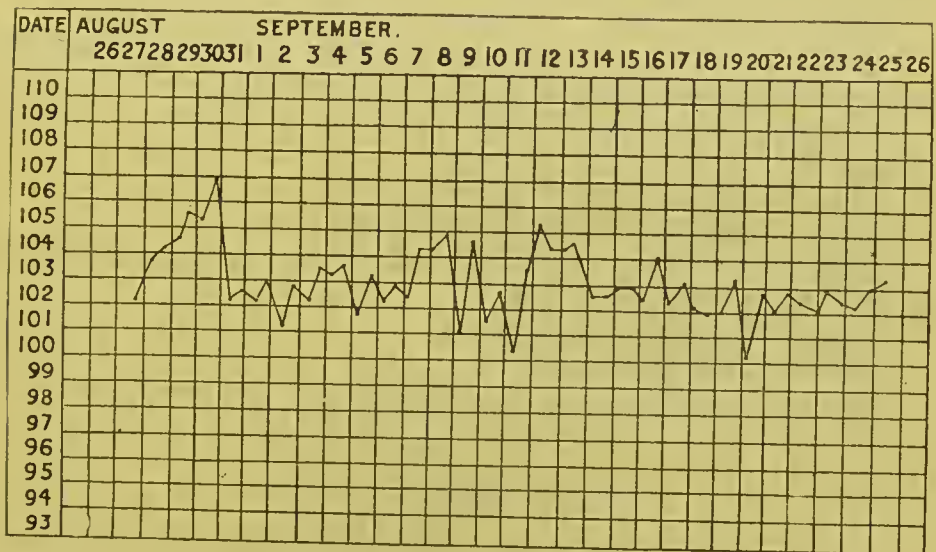
To observe the course of the "Abyssinian fly disease" in a dog.

August 26, 1903. This dog was received to-day from East Africa. It had become sick whilst with the Boundary Commission on the Abyssinian Frontier.

August 27. Blood examined shows many trypanosomes. Animal is thin. Both the corneæ are opaque.

September 7. The animal is getting thinner. There is no œdema of the belly or sheath.

The following chart represents the temperature curve:—



The following table shows the presence or absence of trypanosomes in the blood:—

Date.				Parasites in the blood.		
				Filaria.	Malaria.	Trypanosoma.
1903.						
Aug.	27	—	—	+
"	28	+
"	30	+
Sept.	1	—
"	2	—

Date.					Parasites in the blood.		
					Filaria.	Malaria.	Trypanosoma.
1903.							
Sept.	3	—
"	4	+
"	6	+
"	7	+
"	12	+
"	13	+
"	17	—
"	18	—
"	19	+
"	22	+
"	23	+
"	24	+

September 25, died. Post-mortem 12 hours after death.

The body is much emaciated. Both corneae opaque. No enlargement of superficial glands. No oedema.

On opening the body there is no increase of fluid in pleural, pericardial or peritoneal cavities.

Heart.—Nothing noteworthy.

Lungs.—Both show small embolic areas.

Spleen.—Markedly enlarged, 12 inches by $2\frac{1}{2}$ inches; on section the substance is soft.

Liver.—Nothing noteworthy.

Kidneys.—Both normal.

Glands.—Mesenteric and retroperitoneal are enlarged.

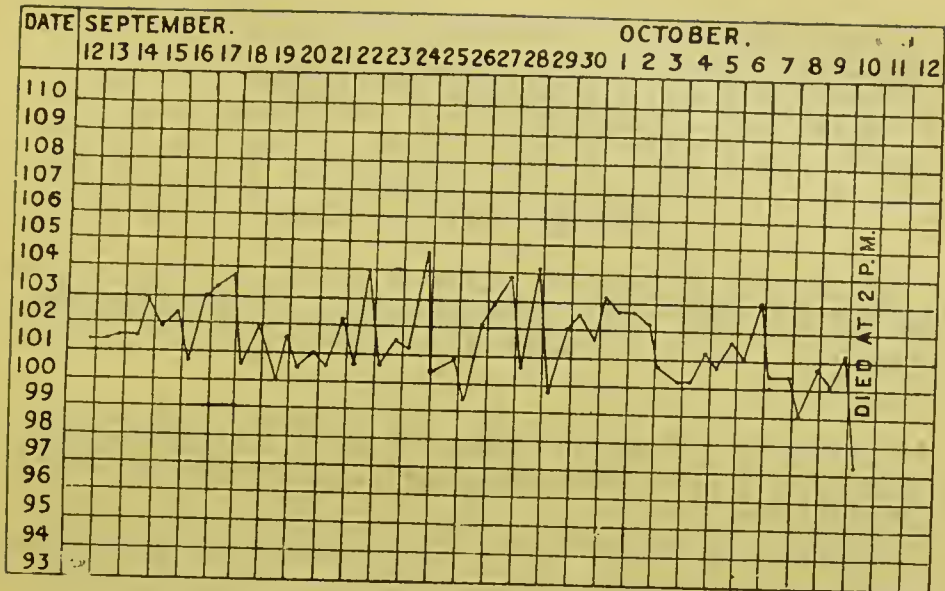
EXPERIMENT 177. DOG.

To note the effects of subcutaneous injection of blood from an animal suffering from the "Abyssinian fly disease" into a dog.

September 12, 1903. Injected subcutaneously 1 c.c. blood from Experiment 160, whose blood contained many trypanosomes.

October 2. The animal is getting thin. The eyes are normal. No oedematous swellings.

The following chart represents the course of the disease:—



The following shows the presence or absence of trypanosomes in the blood:—

Date.					Hb. per cent.	Parasites in the blood.		
						Filar.	Malar.	Tryp.
1903.								
Sept.	12...	—	—	—
"	15...	—	—	+
"	19...	—	—	+
"	21...	78	—	—	+
"	23...	68	—	—	+
"	26...	58	—	—	+
"	29...	59	—	—	+
Oct.	2...	45	—	—	+
"	5...	50	—	—	+
"	9...	38	—	—	+

October 10. Animal died at 2 p.m. Post-mortem $1\frac{1}{2}$ hours after death.

The body is fairly well nourished. There is no oedema. No haziness of corneæ. No increase of fluid in the pleural, pericardial or peritoneal cavities.

Heart.—Shows extensive ecchymosis over left ventricle. There are petechiæ under endocardium of both ventricles. The blood of this organ contains actively motile trypanosomes.

Lungs.—Show many small hæmorrhagic areas. The blood from these areas examined under the microscope shows a number of round bodies about the size of a red corpuscle—these stain blue by Leishman's method and contain one large red dot and several smaller ones.

Liver.—Appears healthy.

(7390)

Spleen.—Considerably enlarged, about 9 inches by 2 inches. On section the pulp is soft.
Kidneys.—Pale, capsule is adherent in places.
Glands.—Are not enlarged.

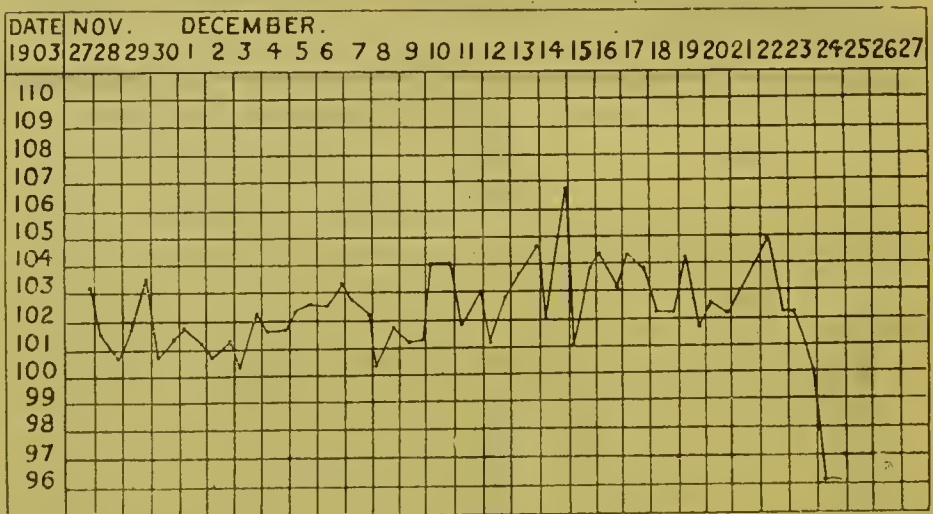
EXPERIMENT 260. DOG.

To note the effect of injection of blood from an ox suffering from the "Abyssinian fly disease," in whose blood the trypanosome was not observed on microscopic examination, into a dog.

November 27, 1903. Injected 20 c.c. of blood subcutaneously from Ox 209, which had not shown trypanosomes in its blood.

December 1. Blood was examined and a filaria, probably *F. imitis*, was observed.

The following chart shows the course of disease:—



The following table shows the presence or absence of filariæ and trypanosomes in the blood:—

Date.		Parasites in the blood.		
		Filar.	Malar.	Tryp.
1903.				
Nov	30
Dec.	1
"	5
"	7
"	8
"	15
"	21
"	24

December 24. Animal died. No post-mortem.

Remarks.—This experiment is of interest as showing that although the ox never showed trypanosomes in the blood on microscopic examination, yet when the blood of this animal was injected into a dog it at once produced the disease, showing that the injection of the trypanosomes into the ox had actually taken and the animal was only partially immune.

C. Injection of blood containing trypanosomes from animals suffering from the Mule disease into dogs.

EXPERIMENT 167. Dog.

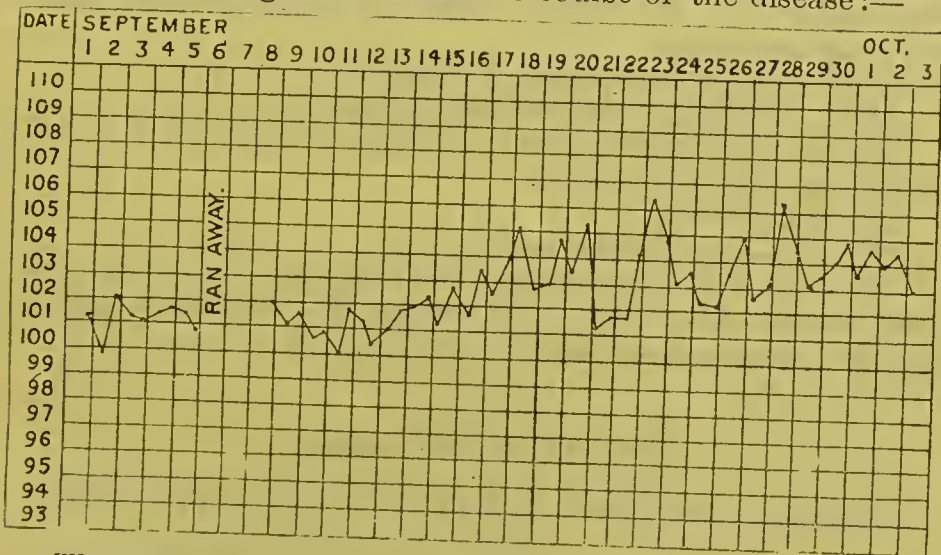
To note the effects of subcutaneous injection of blood from the "Mule Disease" into dog.

September 9, 1903. Injected 18 c.c. of blood from Colonel Sadler's mule subcutaneously.

September 17. The trypanosomes appeared in the blood to-day for the first time, 8 days after inoculation.

October 2. The animal keeps in good condition apparently.

The following chart shows the course of the disease:—



The following table shows the presence or absence of trypanosomes in the blood.

Date.		Hæmo- globin per cent.	Parasites in blood.		
			Filar.	Malar.	Tryp.
1903.					
Sept. 1
" 12
" 14
" 17
" 19

Date.				Hæmo- globin per cent.	Parasites in blood.		
					Filar.	Malar.	Tryp.
1903.							
Sept. 21	95	+
" 23	65	+
" 26	60	+
" 29	60	+
Oct. 2	59	+
" 5	+

October 2. Animal died at 9 a.m. Post-mortem.

The body is well nourished. No opacity of the corneæ. There is no œdema. The lymphatic glands in both axillæ are enlarged.

There is no increase of fluid in the pleural or pericardial cavities, some increase of peritoneal fluid.

Heart.—No petechiæ present. The muscle substance is pale. The blood from this organ examined microscopically shows active trypanosomes.

Lungs.—Both show areas of embolism.

Liver.—Slightly enlarged and appears fatty.

Spleen.—Is enlarged; measures $10\frac{1}{2}$ inches by $2\frac{1}{2}$ inches. On section the substance is soft.

Kidneys.—Are pale.

Glands.—No enlarged in abdomen.

Remarks.—This experiment illustrates the course which the disease takes in a dog. The animal did not show any eye changes, œdema, or marked emaciation.

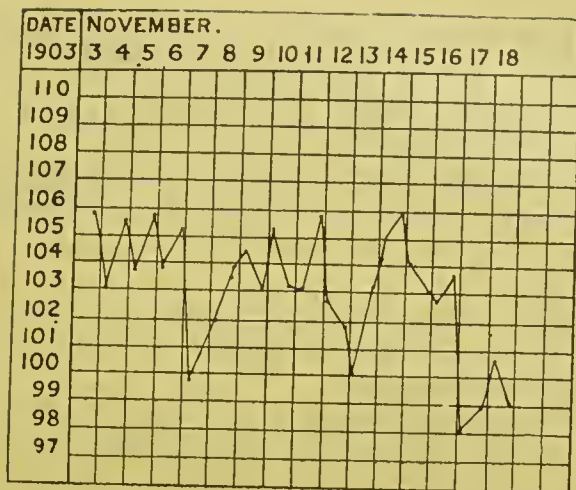
EXPERIMENT 240. JACKAL.

To observe the course of the "mule disease" in a jackal.

November 3, 1903. During the night of November 1 this animal completely devoured a monkey, 232, suffering from the mule disease.

November 5. Animal is seedy to-day; copious semipurulent discharge from eyes.

The following chart shows the course of the disease :—



The following table shows the presence or absence of trypanosomes in the blood :—

Date.				Parasites in the blood.		
				Filaria.	Malaria.	Trypanosoma.
1903.						
Nov.	3	—	—	+
"	8	+
"	9	+
"	17	+

November 18. Died at noon. Post-mortem.

No noteworthy external appearances.

No increase of fluid in pleural, pericardial or peritoneal cavities.

Heart.—There is some jelly-like material at base. Some petechiæ under endocardium of right ventricle.

Lungs.—Right shows two areas of infarction in lower lobe. Both show small round embolic areas.

Liver.—Healthy.

Spleen.—Considerably enlarged, 8 inches by 2½ inches.

Smears from the substance show the presence of a few trypanosomes.

Kidneys.—Both healthy.

Intestines.—Contain a considerable number of anchylostomata.

Remarks.—This experiment illustrates the course of the disease in a jackal.

On the effect of the injection of these Trypanosomes into Baboons, Rabbits, Guinea Pigs, Donkeys and Rats.

EXPERIMENT 220A. DOG-FACED BABOON.

To note the effect of subcutaneous injection of blood from an animal suffering from the "Jinja cattle disease" into a baboon.

June 11, 1904. Experiment 220 having remained negative, 5 c.c. of blood from Experiment 278, suffering from "Jinja cattle disease," was injected.

Trypanosomes never appeared in the blood of this animal.

Remarks.—This experiment shows that the baboon is insusceptible to this variety of trypanosome also.

EXPERIMENT 220. DOG-FACED BABOON.

To note the effect of subcutaneous injection of blood containing trypanosomes from an animal suffering from the "Abyssinian fly disease" into a baboon.

October 8, 1903. Injected 3 c.c. of blood from Dog 177, containing active trypanosomes.

Trypanosomes never appeared in the blood of this animal.

Remarks.—This experiment demonstrates that the dog-faced baboon is insusceptible to this variety of trypanosome.

EXPERIMENT 231. DOG-FACED BABOON.

To note the effect of subcutaneous injection of blood from an animal suffering from the "Mule disease" into a baboon.

October 13, 1903. Injected subcutaneously 8 c.c. of blood from Dog 197.

November 8. Re-injected subcutaneously with 7 c.c. of blood from Jackal 240.

January 19, 1904. Trypanosomes not having appeared in the blood 0.5. c.c. of blood injected subcutaneously from Guinea Pig 182, in whose blood many trypanosomes were present.

Trypanosomes never appeared in the blood of this animal; the temperature remained normal throughout.

Remarks.—This experiment shows that the baboon is not susceptible to this variety of trypanosome also. The baboon is thus immune to all the varieties experimented with.

EXPERIMENT 185. GUINEA PIG.

To note the effects of subcutaneous injection of blood from an animal suffering from the "Jinja cattle disease" with a guinea pig.

September 16, 1903. Injected subcutaneously 1 c.c. blood from Dog 164, containing trypanosomes.

October 15. Trypanosomes appeared in the blood to-day for the first time, twenty-nine days after injection.

The following table shows the presence or absence of trypanosomes in the blood:—

Date.				Temper- ature.	Parasites in the blood.		
					Filaria.	Malar.	Tryp.
1903.							
Sept.	16	—	—	—
"	18	—
"	20	—
"	22	104°	—
"	24	102·2°	—
"	26	103°	—
"	28	—
October	1	—
"	4	—
"	6	—
"	8	—
"	11	—
"	15	+
"	19	—
"	26	+
Nov.	3	+
"	10	+
"	17	+
"	24	+

November 25. Animal died in night. Post-mortem.

The body is not markedly emaciated—a sore over the right hip. No oedematous swellings. The superficial glands are enlarged. No increase of fluid in the pericardial, pleural or peritoneal cavities.

Heart.—Under the epicardium of right ventricle petechiae are present.

Lungs.—Both normal.

Liver.—Nothing noteworthy.

Spleen.—Markedly enlarged and soft on section.

Kidneys.—Both are normal.

Remarks.—Before death the number of trypanosomes present in the blood increased considerably. The disease ran a chronic course in this animal.

EXPERIMENT 316. GUINEA PIG.

To note the effect of subcutaneous injection of blood from an animal suffering from the Jinja cattle disease into a guinea pig.

August 25, 1904. Injected subcutaneously 2 c.c. of blood containing many trypanosomes from Experiment 289.

The following table shows the presence or absence of trypanosomes in the blood:—

Date.				Parasites in the blood.		
				Filaria.	Malaria.	Trypanosoma.
1904.						
August	25	—	—
"	30	—
Sept.	6	—
"	13	—
"	27	—
Oct.	4	+

EXPERIMENT 221. GUINEA PIG.

To note the effect of subcutaneous injection of blood from an animal suffering from the "Abyssinian fly disease" into a guinea pig.

October 8, 1903. Injected subcutaneously 2 c.c. blood from Dog 177, containing active trypanosomes.

December 24, 1903. The trypanosomes not having appeared in the blood, 1 c.c. of blood from Dog 260 was injected subcutaneously.

January 26, 1904. The trypanosomes appeared in the blood to-day for the first time, the thirty-fourth day after the second injection.

August 16, 1904. The animal has an œdematous swelling of the left ear and side of face. It is somewhat emaciated.

The following table shows the presence or absence of trypanosomes in the blood:—

Date.				Parasites in the blood.		
				Fil.	Mal.	Tryp.
1903.						
Oct.	8	...	Injected 2 c.c. blood from D. 177 ...	—	—	—
"	9	—
"	15	—
"	20	—
"	26	—
"	30	—
Nov.	3	—

September 15, 1904. Animal died. Post-mortem.

The body is somewhat emaciated. There is some oedematous swelling about the face. No opacity of corneæ. The superficial glands are generally enlarged. The coat is not out of condition.

No increase of fluid in the pericardial, pleural or peritoneal cavities.

Heart.—Shows nothing noteworthy. The blood of this organ does not contain active trypanosomes, but a few are seen on staining.

Lungs.—Right shows an area of hæmorrhage, smears made from this area show altered trypanosomes; left lung nothing noteworthy.

Liver.—Somewhat congested.

Spleen.—Somewhat enlarged and rather soft on section. Smears from the spleen show altered trypanosomes.

Kidneys.—Nothing noteworthy.

Stomach and Intestines.—Healthy.

Lymphatic glands.—Show general enlargement.

Remarks.—The course of the disease in this animal was remarkably chronic, its duration being nearly a year. The trypanosomes were present in the peripheral blood throughout with the exception of occasional intermissions.

EXPERIMENT 182. GUINEA PIG.

To note the effect of subcutaneous injection of blood from an animal suffering from the "Mule disease" into a guinea pig.

September 13, 1903. Injected 10 c.c. of blood subcutaneously from Mule 179.

November 9. The trypanosomes not having appeared in the blood of this animal, it was reinjected subcutaneously with 5 c.c. of blood from Jackal 240.

November 10. There is some induration at site of inoculation; opened, and necrotic tissue removed.

November 17. Some sloughing of tissue over site of inoculation has occurred.

November 22. Trypanosomes appeared in the blood to-day for the first time, one hundred and ten days after first inoculation, and forty-three days after second.

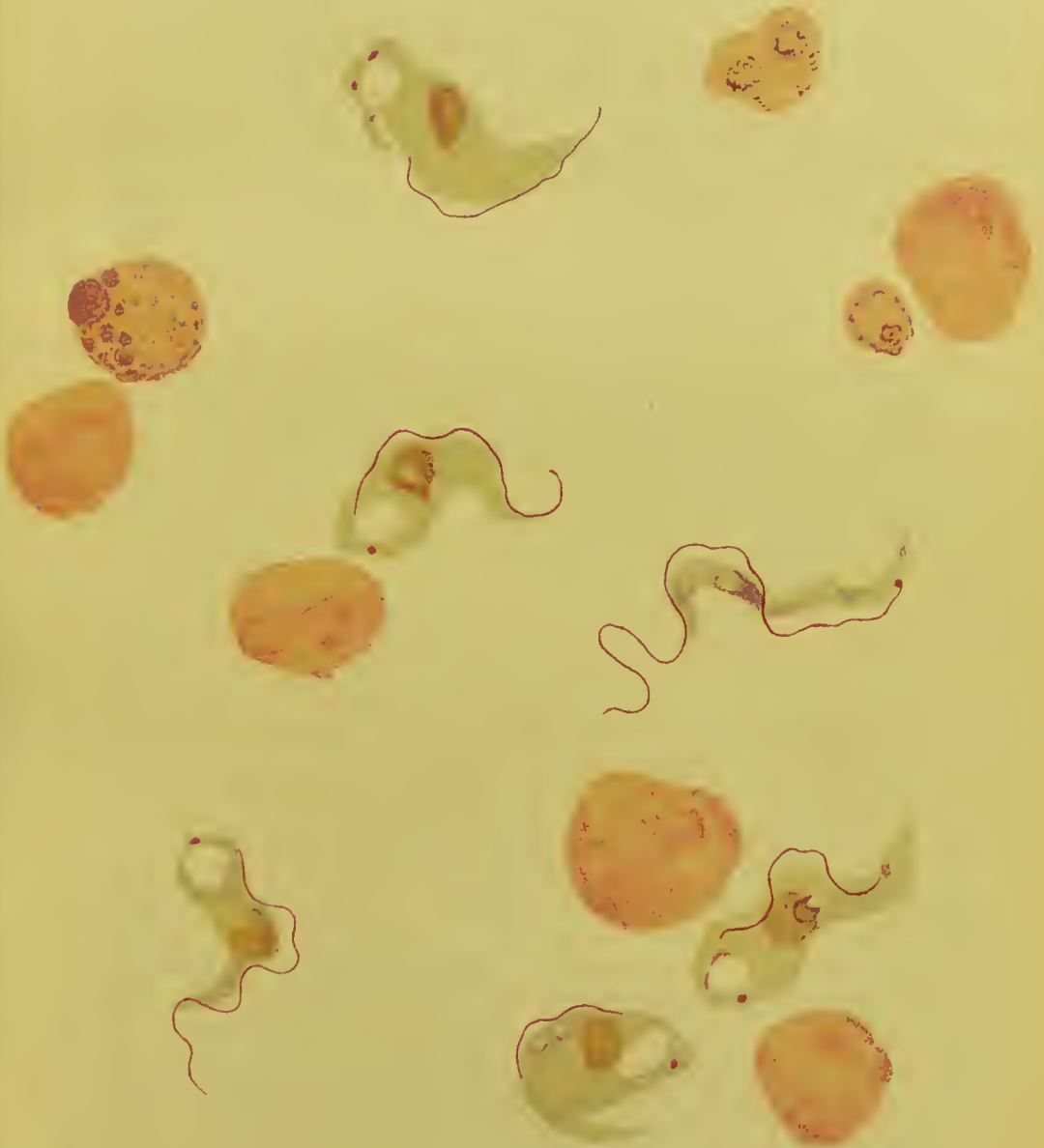
February 2, 1904. Since their appearance in the blood the trypanosomes have become very numerous and have shown peculiar forms; several of these are represented in the coloured plate.

The temperature remained normal throughout.

The following table shows the presence or absence of trypanosomes in the blood:—

BLOOD OF GUINEA PIG.

MULE VARIETY OF TRYPANOSOME.



Date.					Parasites in the blood.		
					Filaria.	Malaria.	Trypanosoma.
1903.							
Sept.	15	—	—	—
"	18	—
"	20
"	22	—
"	24
"	26	—
"	28	—
Oct.	1	—
"	4	—
"	6	—
"	8	—
"	10	—
"	15	—
"	19	—
"	26	—
"	30	—
Nov.	3	—
"	9	—
"	10	—
"	17	—
"	24	—
Dec.	1	—
"	8	—
"	15	—
"	22	+
"	29	+
1904.							
Jan.	6	+
"	11	+
"	12	+
"	19	+
"	26	+
Feb.	2	+
"	9	+
"	14	+

February 14, 1904. Animal died in the night. Post-mortem.

The body is not emaciated.

There is no increase of fluid in the pleural, pericardial or peritoneal cavities.

Heart.—Shows an extensive area of hæmorrhage over left ventricle—small point of hæmorrhage under endocardium of left ventricle. The blood of this organ shows very few trypanosomes.

Lungs.—Left shows an extensive area of hæmorrhage under pleura over lower lobe. Right shows a number of minute embolic areas scattered through it.

Liver.—Nothing noteworthy.

Spleen.—Distinctly enlarged, and on section showed a

number of greyish sago grain-like points. Examination of the pulp showed trypanosomes, but most of them were considerably modified from the normal appearance.

Kidneys.—Right showed small area of infarction; left nothing noteworthy.

Glands.—A few retroperitoneal were enlarged.

Remarks.—This experiment illustrates the course of this disease in the guinea pig. The most noteworthy points were the long duration of the disease, the very slight manifestations clinically, the late appearance of the trypanosomes in the peripheral blood, the large number of parasites present and their peculiar forms.

EXPERIMENT 289. RABBIT, YOUNG.

To note the effect of subcutaneous injection of blood from an animal suffering from the Jinja cattle disease into a rabbit.

May 6, 1904. Injected subcutaneously 1 c.c. of blood containing many trypanosomes from monkey, Experiment 263.

May 17. Trypanosomes are present in the blood eleven days after inoculation.

August 23. Animal has got opacity of both corneæ.

The fur is shed in places and the coat is much out of condition. The animal is considerably emaciated.

The temperature remained about normal until August 25, 1904 (the day of its death) when it fell 93.5° .

The following table shows the presence or absence of trypanosomes in the blood:—

				Parasites in the blood.		
Date.				Filaria.	Malaria.	Trypanosoma.
1904.						
May	10	—	—	—
"	17	—	+
"	31	+
June	14	+
"	22	+
"	28	+
July	12	+
"	19	+
"	26	+
Aug.	2	+
"	9	+
"	16	+
"	23	+
"	25	+

August 25, 1904. Animal died to-day. Post-mortem at once.

The body is emaciated. Both corneæ are opaque. The coat is much out of condition. The lymphatic glands are not enlarged.

There is no increase of fluid in the pericardial, pleural or peritoneal cavities.

Heart.—Nothing noteworthy. The blood of this organ contains many active trypanosomes.

Lungs.—Both healthy.

Liver.—Nothing noteworthy.

Spleen.—Not enlarged.

Lymphatic glands.—Not enlarged.

Remarks.—This experiment demonstrates the course of this disease in a rabbit. It runs a somewhat chronic course. The animal, however, shows very marked signs of deterioration of health.

EXPERIMENT 295. RABBIT.

To note the effect of subcutaneous injection of blood from an animal suffering from the "Mule disease" into a rabbit.

May 20, 1904. Injected subcutaneously 5 c.c. of blood from Monkey 276 into this rabbit.

August 16. Trypanosomes are present in the blood of this animal to-day, fifty-seventh day after injection.

The following table shows the presence or absence of trypanosomes in the blood:—

Date.				Parasites in the blood.		
				Filaria.	Malaria.	Trypanosoma.
1904.						
May	31	—	—
June	14	—
"	21	—
"	28	—
July	12	—
"	19	—
"	26	—
Aug.	2	—
"	9	—
"	16	+
"	23	+
"	30	—
Sept.	6	—
"	13	—

EXPERIMENT 179. COLONEL SADLER'S MULE.

September 9, 1903. This animal has been sick since July 3, 1903. It has been in Africa about five years; at first it was in East Africa, and for the last eighteen months has been in

Uganda. It remained well until recently, when it commenced to have swelling of the glands and fever. It eats well. It is getting thin. There is no swelling of the sheath. The blood was examined and trypanosomes were found to be present.

September 13. Animal was brought up to the laboratory this morning. It was very weak and fell down; it never rose again.

The temperature oscillated between 105° and 107°.

The following table shows the presence or absence of trypanosomes in the blood:—

Date.				Parasites in the blood.		
				Filar.	Malar.	Tryp.
1903.						
Sept.	9	—	—	+
"	12	—
"	13	—

September 13. Animal died. Post-mortem at once.

The animal is emaciated, no opacity of corneæ—no swelling of sheath, no enlarged superficial glands. There is no increase of fluid in the pericardial, pleural or peritoneal cavities.

Heart.—No jelly-like material round the base. A few petechiæ under epicardium, also under the endocardium of right ventricle. The heart muscle is pale. The blood is very watery; inoculated into two monkeys, rat and guinea pig; 10 c.c. blood was centrifuged, but no trypanosomes were seen.

Lungs.—Both normal.

Spleen.—Enlarged, weighs about 14 lbs.; somewhat congested.

Kidneys.—Both normal.

Glands.—Not enlarged in mesentery or retroperitoneally.

Remarks.—The above case is of interest as it brought under observation a disease in mules caused by a trypanosoma. The trypanosoma met with in this disease has been fully investigated.

Although no trypanosomes could be seen microscopically on two occasions in the blood of this animal, yet when injected into other animals the trypanosomes appeared in due course.

EXPERIMENT 278. DONKEY (*Masai*).

To note the effect of subcutaneous injection of blood from an animal suffering from "Jinja cattle disease" into a Masai donkey.

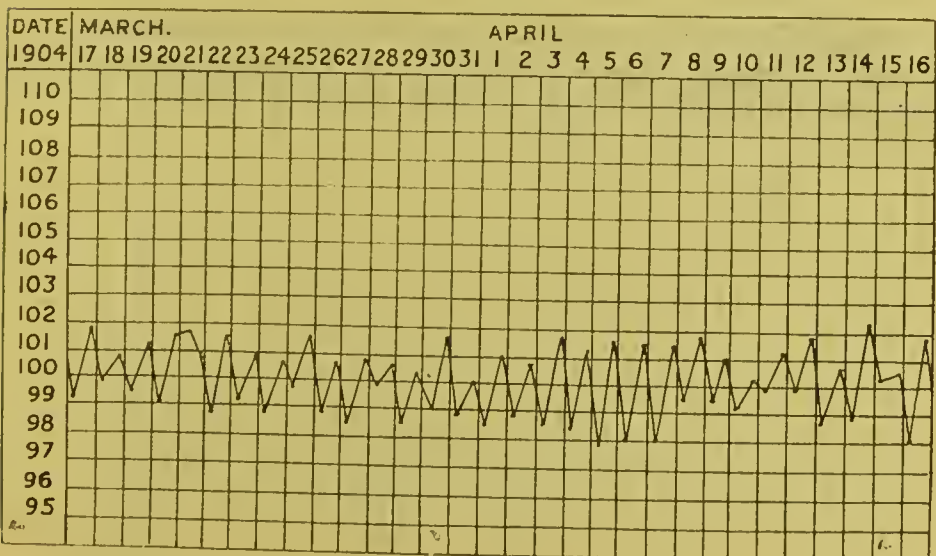
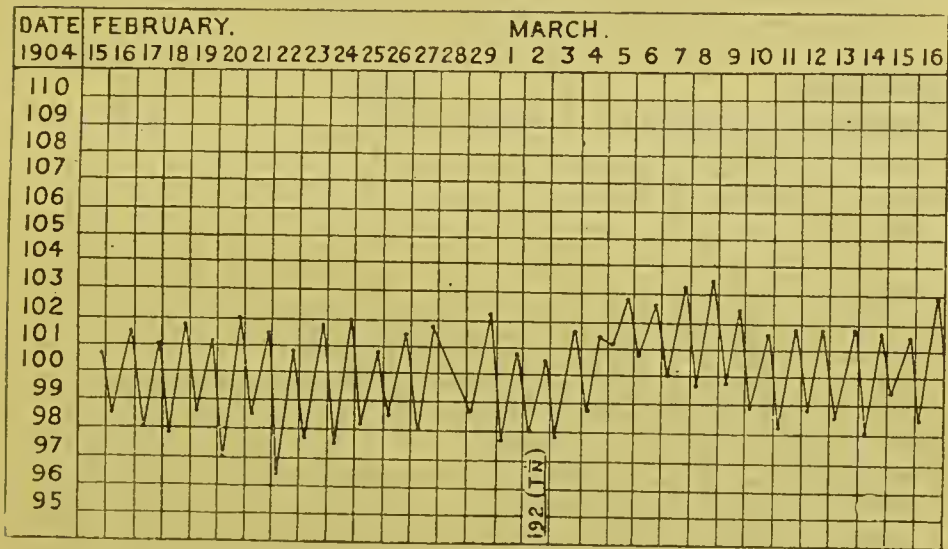
March 2, 1904. Injected subcutaneously 10. c.c. of blood from goat, Experiment 192.

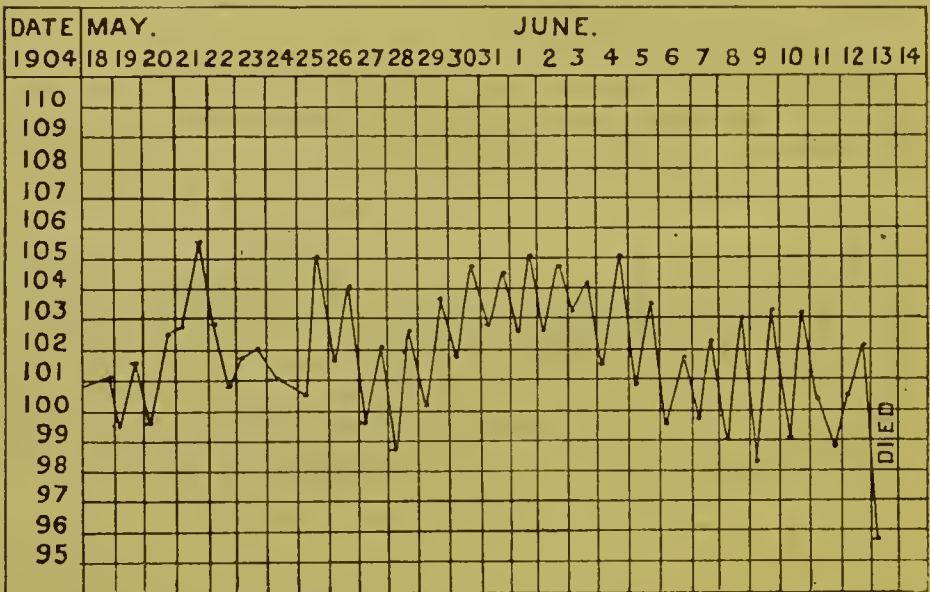
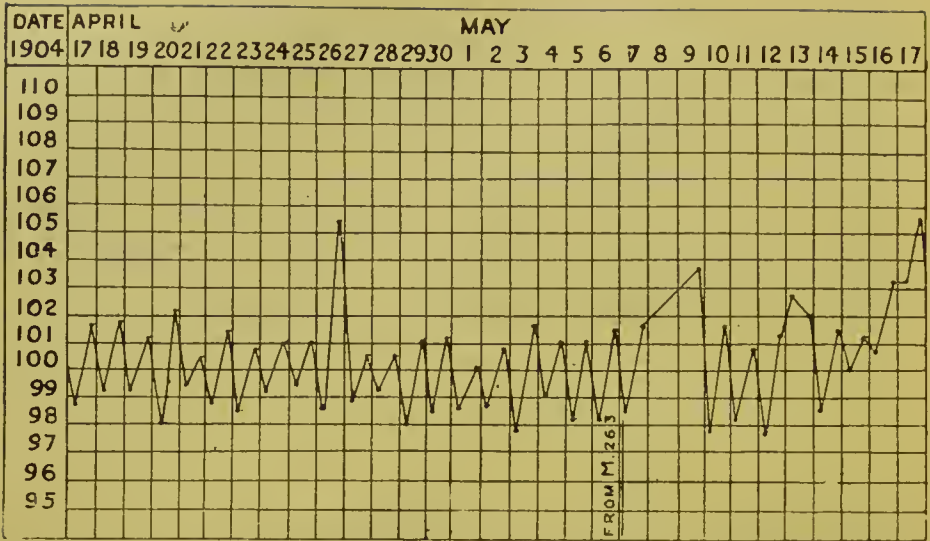
May 6. Trypanosomes not having appeared in the blood, the animal was reinjected with 4 c.c. of blood subcutaneously from Experiment 263, in whose blood at the time of injection there were 38,000 trypanosomes per c.mm.

May 18. Trypanosomes appeared in the blood to-day, the thirteenth day after inoculation.

June 11. Animal is very sick and unable to rise. Its coat is rough, conjunctivæ very pale. Breathing is rapid and shallow. No œdematous swellings.

The following chart shows the course of the disease :—





The following table shows the result of enumeration of the blood corpuscles, the percentage of hæmoglobin and the presence or absence of trypanosomes in the blood :—

Date.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in blood.		
			P.N.	S.M.	L.M.	E.		Filar.	Malar.	Tryp.
1904.										
Feb. 24	-	-	-
March 9	-
" 16	-
" 23	-
" 30	-
April 7	-
" 20	-
" 27	-
May 4	-
" 11	-
" 18	-
" 24	-
June 1	+
" 8	+
" 11	+
	2,350,000	22,500	72	13	14	1	24	+

June 13. Animal died at 12.30 p.m. Post-mortem at once.

The body is not emaciated. No œdematous swellings. No opacity of corneæ. A general enlargement of superficial glands is present. No increase of fluid in pleural, pericardial or peritoneal cavities.

Heart.—There is some jelly-like material round base. Petechiæ under epicardium and endocardium.

Lungs.—Both healthy.

Liver.—Enlarged and congested.

Spleen.—Somewhat enlarged and congested; smears from this organ show broken-down trypanosomes.

Kidneys.—Both healthy.

Intestines.—Healthy.

Glands.—In retroperitoneal region are enlarged. Smears from the glands show the presence of broken-down trypanosomes.

Remarks.—The first injection from the goat did not take in this animal. After the second injection, however, trypanosomes appeared on the 13th day, and he died on the 26th day. The blood examination showed a marked diminution in the number of red corpuscles and hæmoglobin. The duration of the disease after the appearance of the trypanosomes was much shorter than in the case of the other varieties of animal trypanosomes.

EXPERIMENT 222. DONKEY (*Masai*).

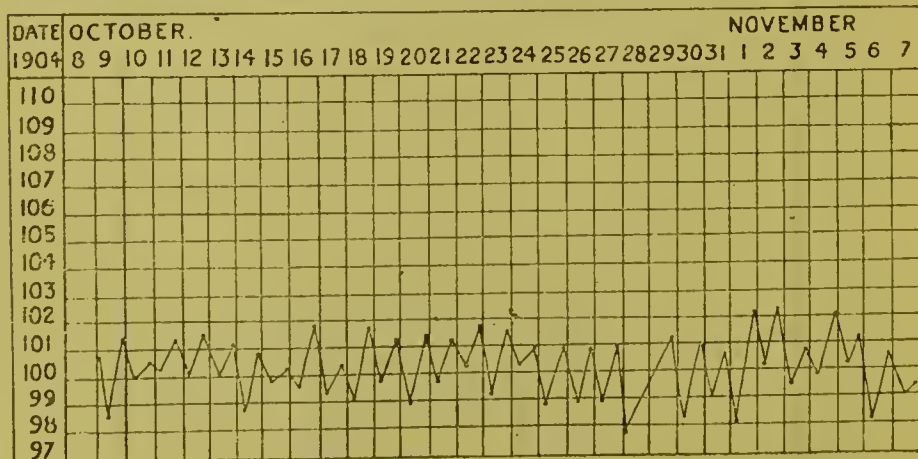
To note the effect of subcutaneous injection of blood from an animal suffering from the "Abyssinian fly disease" into a donkey.

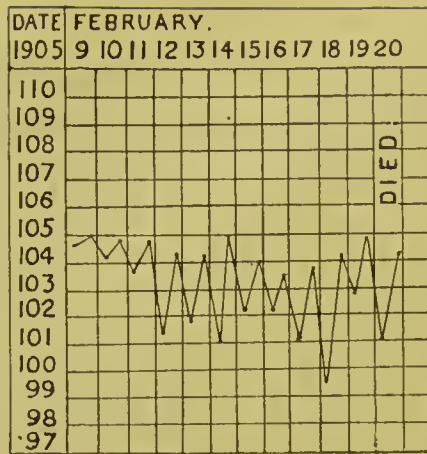
October 8, 1903. Injected 5 c.c. blood from dog, Experiment 177, containing active trypanosomes.

November 23. Trypanosomes not having appeared in the peripheral blood, 10 c.c. of blood was taken and injected into dog, Experiment 256.

December 1. Trypanosomes appeared to-day in the blood of the dog, Experiment 256.

The following chart shows the course of the disease :—





The following table shows the presence or absence of trypanosomes in the blood :—

Date.				Parasites in the blood.		
				Filar.	Malar.	Tryp.
1904.						
Oct. 8	—	—	—
„ 16	—
„ 21	—
„ 28	—
Nov. 4	—
„ 11	—
„ 18	—
„ 25	—
Dec. 2	—
„ 9	—
„ 16	—
„ 23	—
„ 30	—
1905.						
Jan. 7	—
„ 13	—
„ 20	—
„ 27	—
Feb. 3	+
„ 9	—
„ 17	—
„ 21	+

February 21. Animal died last night. Post-mortem.

There is no opacity of corneæ. There is slight general enlargement of superficial lymphatic glands. The coat is out of condition, but emaciation is not marked. No œdematous swellings. No increase of fluid in the pleural, pericardial or peritoneal cavities.

Heart.—A few small petechiæ on surface, also under

endocardium of all the cavities there are numerous petechiæ. There is no jelly-like material at base. Muscle substance is pale.

Lungs.—Vessels are plugged with discoloured elots.

Liver.—Nothing noteworthy.

Spleen.—Slightly enlarged—firm on section.

Kidneys.—Nothing noteworthy.

Brain.—No noteworthy change, naked eye.

Glands.—Some enlargement of the glands along the great vessels of the neck. Smears made from the glands on staining show trypanosomes apparently breaking down.

Remarks.—This experiment is of considerable interest, as it demonstrates the course of this disease (Abyssinian) in a donkey. As compared with the "mule disease" in the donkey it runs a more chronic course; the trypanosomes were only found once in the peripheral blood, but their presence was demonstrated by injection of a susceptible animal, Dog 256.

EXPERIMENT 229. DONKEY (*Masai*).

To note the effect of subcutaneous injection of blood from an animal suffering from the "mule disease" into a donkey.

October 13, 1903. Injected 10 c.e. of blood from heart of Dog 197 post-mortem; no active trypanosomes were seen.

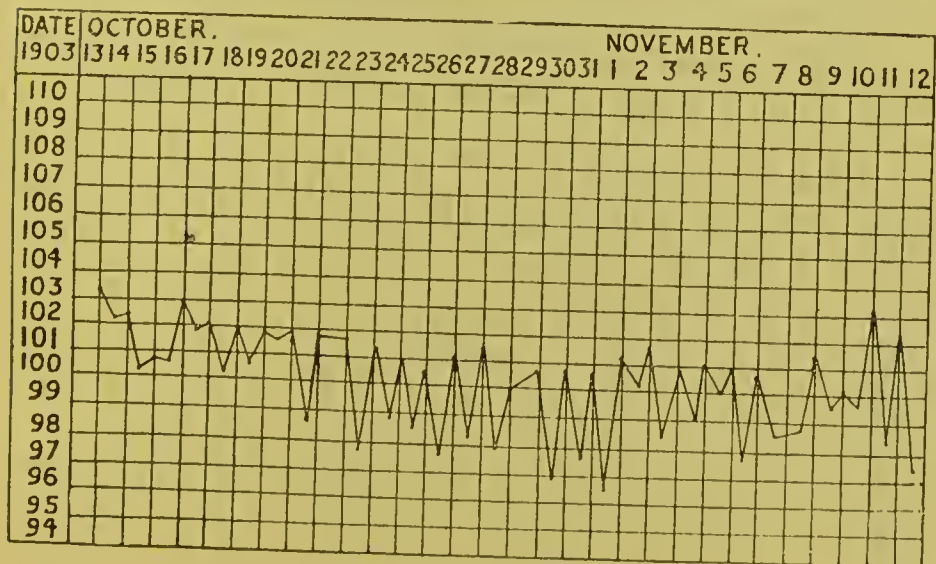
November 9. Injected 5 e.e. of blood from Jaekal 240, containing active trypanosomes.

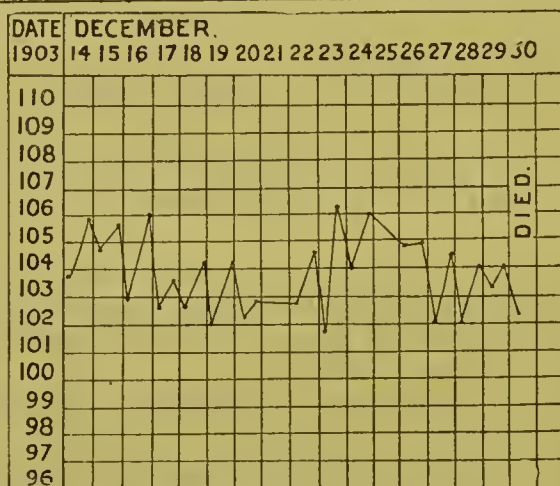
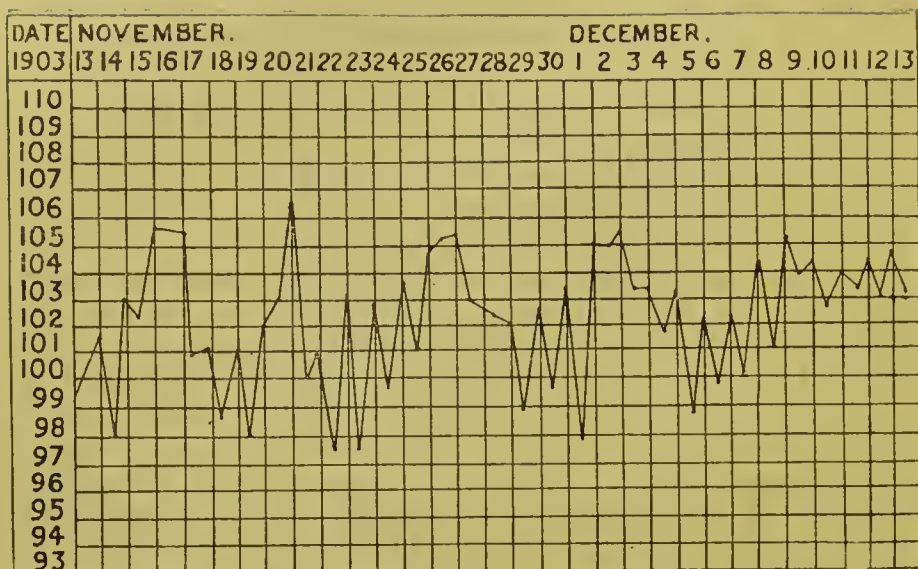
November 25. 'Trypanosomes' appeared in the blood to-day,
16 days after reinjection.

December 26. Animal is distinctly seedy to-day. He is not taking his food. His head is drooping and coat is staring.

December 27. Now disinclined to move from one place. He is not taking his food and looks very ill.

The following chart shows the course of the disease:—





The following table shows the presence or absence of trypanosomes in the blood :—

Date.				Parasites in the blood.		
				Filaria.	Malaria.	Trypanosoma.
1903.						
Oct.	13	—	—	—
"	21	—
"	28	—
Nov.	4	—
"	11	—
"	18	—
"	21	—
"	22	—
"	25	+
"	29	+
Dec.	2	+
"	9	+
"	16	+
"	23	+
"	29	+

December 30. The animal died at 12 noon to-day. Post-mortem.

The body is not much emaciated. No œdematous swellings. No opacity of corneæ. Conjunctivæ very pale.

No increase of fluid in the pericardial, pleural or peritoneal cavities.

Heart.—On opening the pericardium, a red band was seen stretching across the left ventricle; this was composed of an agglomeration of minute petechiæ. A number of other petechiæ were distributed over the surface of the heart. The endocardium shows numerous petechiæ. The myocardium is pale.

Lungs.—Show a few hæmorrhages under the pleural membrane. No infiltration of jelly-like substance.

Liver.—Nothing noteworthy.

Spleen.—Slightly enlarged, section congested; smears stained show altered trypanosomes.

Kidneys.—Both very pale.

Glands.—Not markedly enlarged. Smears examined after staining show altered trypanosomes.

Brain.—Preserved for minute investigation; showed no naked eye change.

Remarks.—This is a very interesting experiment, proving as it does that the donkey, *although a Masai one*, is not immune, at least to this variety of trypanosome. The animal did not present the normal features met with in Nagana, viz., emaciation, œdematous swelling or opacity of corneæ. This animal was previously repeatedly injected with blood from a case of "trypanosoma fever," but it remained refractory. This experiment, therefore, suggests that the *Trypanosoma gambiense* differs from this variety of trypanosoma.

EXPERIMENT 175. RAT.

To note the effects of subcutaneous injection of blood from an animal suffering from the "Jinja cattle disease" into a rat.

September 7, 1903. Injected a few drops of blood from Experiment 164, containing many trypanosomes.

September 12. The trypanosomes appeared in the blood for the first time.

The following table shows the presence or absence of trypanosomes in the blood:—

Date.				Parasites in the blood.		
				Filaria.	Malaria.	Trypanosoma.
Sept. 7	1903.					
" 10	—	—	—
" 12	—
" 14	+
" 14	+

September 14. Animal died. Post-mortem.

Organs showed nothing noteworthy. The blood from the heart contained active trypanosomes.

EXPERIMENT 173. RAT.

To note the effect of subcutaneous injection of blood from an animal suffering from the "Abyssinian fly disease" into a rat.

September 7, 1903. Injected 0.5 e.e. blood from Experiment 160, dog, whose blood contained many trypanosomes.

September 10. The trypanosomes appeared in the blood of this animal to-day, the third day after inoculation.

The following table shows the presence or absence of trypanosomes in the blood :—

Date.					Parasites in the blood.		
					Filaria.	Malaria.	Trypanosoma.
1903.							
Sept. 7	—	—	—
" 10	+
" 12	+
" 15	+

September 17. Animal died. Post-mortem several hours after death.

Heart.—Shows nothing noteworthy. The blood from this organ contained no living trypanosomes.

Lungs.—Left shows slight congestion. Right is healthy.

Liver.—Nothing noteworthy.

Spleen.—Slightly enlarged.

Kidneys.—Nothing noteworthy.

Remarks.—The disease ran an acute course in this animal, dying ten days after inoculation.

EXPERIMENT 190. RAT.

To note the effect of subcutaneous injection of blood from an animal suffering from the "Abyssinian fly disease" into a rat.

September 19, 1903. Injected subcutaneously 2 e.e. blood from dog, Experiment 160.

September 26. The blood was examined and found to contain trypanosomes; seventh day after inoculation.

The following table shows the presence or absence of trypanosomes in the blood :—

Date.					Parasites in the blood.		
					Malaria.	Filaria.	Trypanosoma.
1903.							
Sept.	19	—	—	—
"	21	—
"	22	—
"	23	—
"	24	—
"	26	+
"	28	+
Oct.	2	+
"	3	+

October 3. The animal died. Post-mortem.

There are no œdematous swellings present. There is no increase of fluid in pericardial, pleural or peritoneal cavities.

Heart.—Nothing noteworthy. The blood of this organ contains a few trypanosomes which are somewhat vacuolated in appearance.

Lungs.—Both healthy.

Spleen.—Is enlarged and congested.

EXPERIMENT 208. RAT.

To note the effect of subcutaneous injection of blood from an animal suffering from the "mule disease" into a rat.

September 28, 1903. Injected 1.5 c.c. blood from Monkey 180 containing active trypanosomes.

The following table shows the presence or absence of trypanosomes in the blood :—

Date.					Parasites in the blood.		
					Malaria.	Filaria.	Trypanosoma.
1903.							
Sept.	30	—	—	—
Oct.	1	+
"	12	+
"	24	+
Nov.	3	+
"	10	+
"	17	+
"	24	+
Dec.	1	+
"	8	+
"	15	+

December 15, 1903. Animal died. Post-mortem.

No marked emaciation. The superficial glands are not enlarged.

Heart.—Shows hæmorrhages into muscular wall of left ventricle, otherwise healthy. The blood of this organ did not contain active trypanosomes.

Lungs.—Both healthy.

Liver.—Slightly enlarged and very pale.

Spleen.—Distinctly enlarged, pale, soft on section.

Remarks.—This experiment illustrates the fact that the disease may run a remarkably chronic course in rats. The trypanosomes were present in the peripheral blood throughout the disease.

EXPERIMENT 187. RAT.

To note the effects of injection of blood from an animal suffering from the "mule disease" into a rat.

September 19, 1903. Injected subcutaneously 1 c.c. blood from Dog 167, containing active trypanosomes.

September 24. The blood of the rat showed the presence of trypanosomes to-day, five days after injection.

The following table shows the presenee or absence of trypanosomes in the blood:—

Date.					Parasites in the blood.		
					Filaria.	Malaria.	Trypanosoma.
1903.							
Sept.	19	—	—	—
"	20	—
"	21	—
"	22	—
"	23	—
"	24	+
Oct.	4	+
"	11	+

October 11. Animal died at 12 noon. Post-mortem.

The body is not emaciated. No oedematous swellings. The superficial glands are enlarged. No increase of fluid in pericardial, pleura or peritoneal cavities.

Heart.—Petechiæ present on surface. The blood from this organ shows very many active trypanosomes.

Lungs.—Both healthy.

Liver.—Nothing noteworthy.

Spleen.—Markedly enlarged. On staining a film various modifications in shape of the trypanosomes from the normal are observed, some being swollen and vacuolated, others are quadrilateral or circular; the macro and micro-nuclei stain well.

Kidneys.—Nothing noteworthy.

Lymphatic glands.—The retroperitoneal are considerably enlarged.

On the effect of the injection of these Trypanosomes into Oxen, Sheep, and Goats.

In addition to injection of blood containing each "strain" of trypanosoma into these animals, other experiments were performed to determine whether any difference could be made out between the various "strains" of trypanosoma; advantage was taken of the fact that these animals (oxen, goats and sheep) proved refractory to two "strains" of trypanosoma to subsequently inject them with blood containing another "strain."

In this way a difference was established between the varieties of trypanosomes under observation.

The results are as follows:—

EXPERIMENT 162. BLACK BULLOCK.

To note the effects of subcutaneous injection of blood from an animal suffering from the "Jinja cattle disease" into an ox.

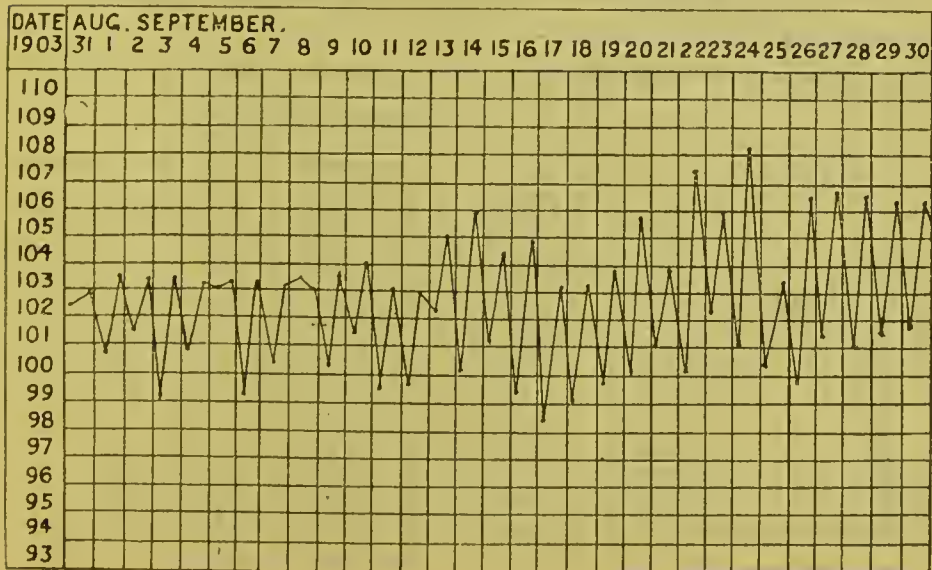
September 9, 1903. Injected 10 c.c. blood subcutaneously from Dog 164 containing trypanosomes of the "Jinja cattle disease."

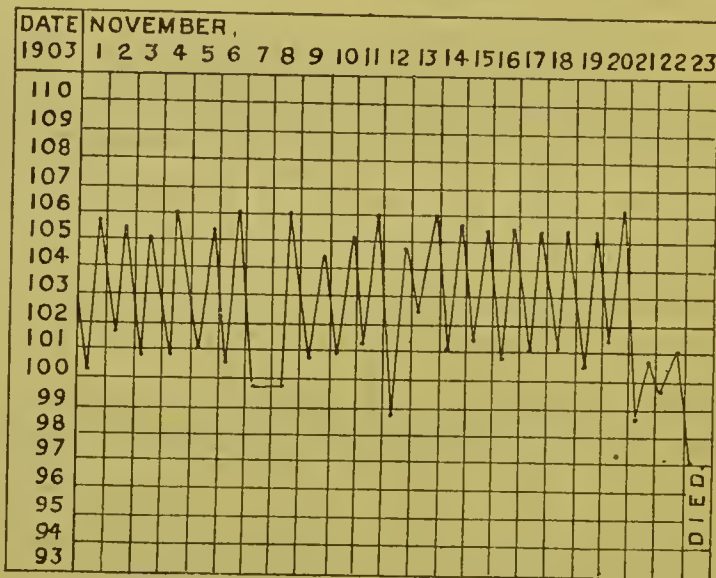
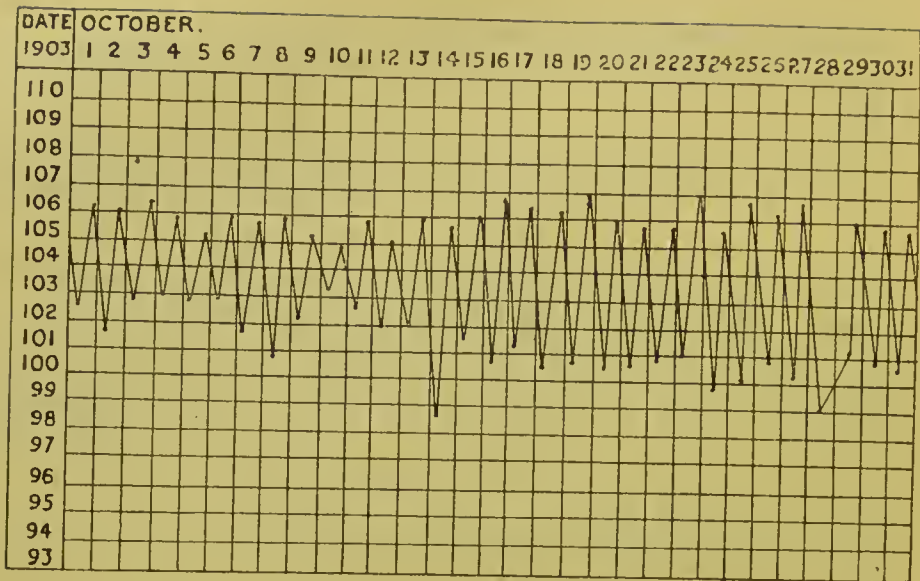
September 21. The animal has been getting thinner lately. Trypanosomes found in the blood to-day twelve days after injection.

October 8. The animal has been noticed to be lying down a good deal. A slight haziness of the corneæ of both eyes is visible.

November 21. The animal appears very sick to-day, is lying down and cannot be got to rise. Pulse very weak and rapid. This evening appears in moribund condition.

The chart represents the course of the disease:—





The following table shows the presence or absence of trypanosoma in the blood :—

Date.		Parasites in the blood.		
		Filaria.	Malaria.	Trypanosoma.
1903.				
Sept. 9	...	—	—	—
„ 12	—
„ 15	—
„ 18	—
„ 21	+
„ 23	+
„ 26	+
„ 28	+

Date.					Parasites in the blood.		
					Filaria.	Malaria.	Trypanosoma.
1903.							
Oct.	2	+
"	6	+
"	9	+
"	12	+
"	15	+
"	19	+
"	21	+
"	28	+
Nov.	4	+
"	11	+
"	18	+
"	21	+

November 23. Animal died at 12 p.m. Post-mortem at once.

There was slight opacity of the corneæ of both eyes. The supraclavicular lymphatic gland is enlarged and congested, also glands in the neck.

On opening the body some increase of fluid in pericardial cavity is noticed, fluid in pleural and peritoneal cavities not increased.

Heart.—Round the base there is well-marked jelly-like substance. There are petechiæ under epicardium of right auricle, also under endocardium of left ventricle and right auricle. Heart's blood is watery.

Lungs.—Show some jelly-like substance at the division of the main bronchi.

Spleen.—Distinctly enlarged, on section is congested.

Liver and Kidneys.—Nothing noteworthy.

Brain.—Distinct increase of subarachnoid fluid, giving a cloudy appearance to the brain.

Remarks.—This is an important experiment, as it exactly reproduces both clinically and pathologically the features of the disease observed in the cattle originally seen at Jinja. The duration is the same, viz., three months. The mode of death was similar, the animal being apparently not very seriously ill, no emaciation or alteration of coat, and only very slight opacity of corneæ. It lay down about two days before its death and never rose again. It died in fairly good condition as the Jinja cattle died. The post-mortem appearances were also similar to those met with in the Jinja cattle. The appearance of the brain was curious, being not unlike that met with in sleeping sickness cases; portions were preserved for future examination.

EXPERIMENT 209. Ox.

To note the effect of subcutaneous injection of blood from an animal suffering from the "Abyssinian fly disease" into an ox.

October 8, 1903. Injected subcutaneously 5 c.c. of blood from Dog 177 into this ox.

November 27. Injected subcutaneously 20 c.c. of blood from this ox into Dog 260.

December 2. Again injected subcutaneously 15 c.c. of blood from Dog 256 into this ox.

December 9. Trypanosomes have appeared in the blood of Dog 260 to-day.

January 26, 1904. Again injected subcutaneously 20 c.c. of blood from this ox into Dog 277.

February 23. Trypanosomes appeared in the blood of Dog 277.

September 30. The animal shows some slight emaciation, but no trypanosomes have appeared in its peripheral blood. Injected 20 c.c. of blood subcutaneously into Monkey 319.

The temperature oscillated between 98° and 105°.

Trypanosomes never appeared in the blood of this animal.

EXPERIMENT 202. Ox.

To note the effect of subcutaneous injection of blood from an animal suffering from the "mule disease" into an ox.

September 28, 1903. Injected subcutaneously 6 c.c. of blood from monkey, Experiment 180.

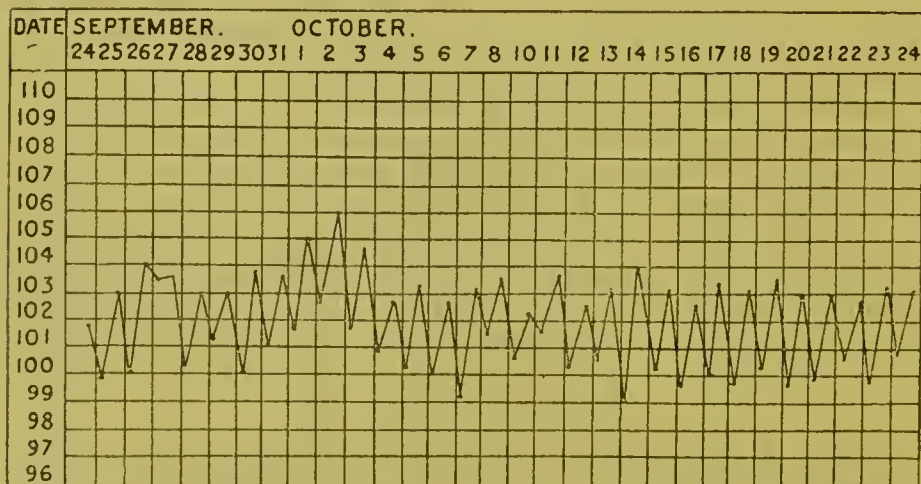
October 15. 10 c.c. blood were centrifuged, no active trypanosomes were found.

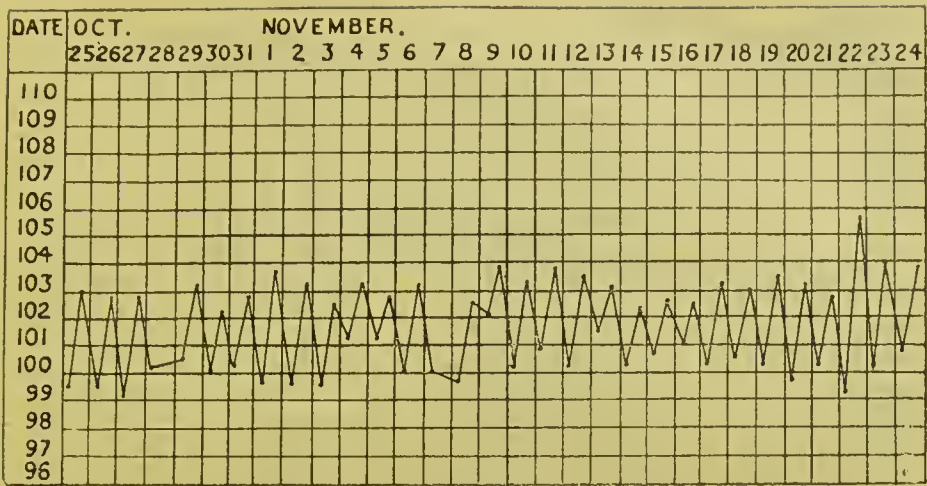
November 2. Injected subcutaneously 20 c.c. of blood from this animal into a dog, Experiment 239.

November 9. Injected subcutaneously 5 c.c. blood from jackal, Experiment 240.

November 10. Trypanosomes appeared to-day in the blood of Dog 239 which was injected with blood from this animal.

The following chart shows the course of the disease:—





This animal was then used for the following observation:—

To note the effect of injection of blood from an animal suffering from another variety of trypanosomic disease (Jinja) into an animal previously inoculated with blood from animal affected with the “mule disease,” but in whose blood the parasites had not appeared.

November 21. Injected subcutaneously 25 c.c. blood from Ox 162, which was dying.

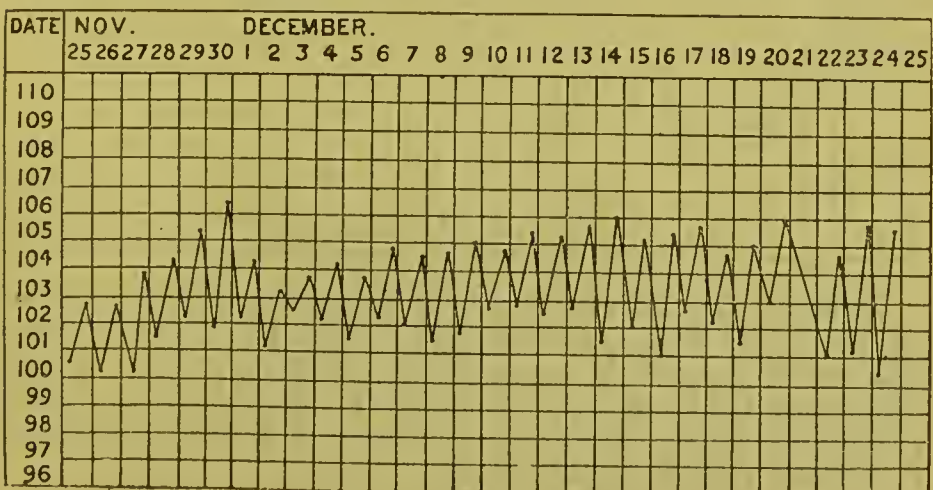
December 2. Trypanosomes appeared in the blood to-day for the first time. This is the 12th day after the injection of the blood. The interval corresponds exactly to the incubation period in the “Jinja disease”; compare Experiment 162.

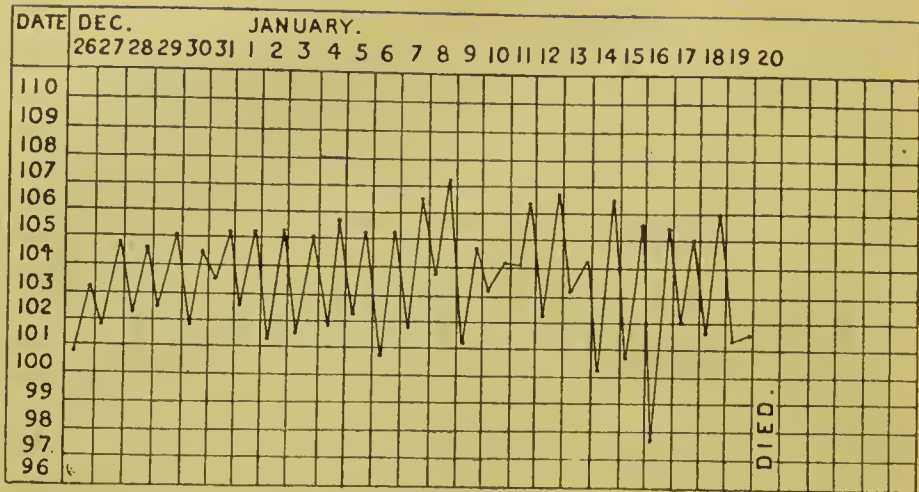
December 15. The animal appears thinner, the coat is not staring.

January 13, 1904. The animal seems less vigorous than before, otherwise there is no noteworthy change.

January 19. The animal is unable to rise to-day. The conjunctivæ are very pale. There is not much emaciation.

The following chart shows the course of the disease:—





The following table shows the presence or absence of trypanosomes in the blood:—

Date.		Parasites in the blood.		
		Filaria.	Malaria.	Trypanosoma.
1903.				
Sept. 25	...	—	—	—
Oct. 2	—
" 6	—
" 10	—
" 13	—
" 15	—
" 19	—
" 21	—
" 28	—
Nov. 4	—
" 11	—
" 18	—
" 21	—
" 25	—
Dec. 2	+
" 9	+
" 16	+
" 23	+
" 30	+
1904.				
Jan. 6	+
" 13	+
" 19	+

January 20. The animal died at 12.30 p.m. Post-mortem at once. The body is not emaciated and the coat is not staring. The superficial glands are generally enlarged. There is slight opacity of both corneæ. No jelly-like material seen in subcutaneous tissue. There is no increase of fluid in the pleural, pericardial or peritoneal cavities.

Heart.—There is some jelly-like material round the base. A

few petechiae on the surface of the heart, also under endocardium of both ventricles. The muscle substance is pale. The blood from this organ contains active trypanosomes.

Lungs.—In both areas of infarction are seen; they are wedge-shaped and measure about one inch across.

Spleen.—Slightly enlarged and congested.

Kidneys.—Both apparently healthy.

Brain.—Some injection of superficial vessels, sub-arachnoid fluid increased.

Glands.—Along the line of the aorta and iliac vessels are enlarged and on section appeared congested.

Remarks.—This experiment is an important one, and forms one of a series designed to observe whether there was any difference in the effect on cattle between the “Jinja” and the “mule” trypanosomes.

This animal was originally inoculated with the “mule” variety of trypanosome, and for two months, although reinjected, never showed trypanosomes in its peripheral blood. Its blood was, however, infectious, and when injected into a dog, the trypanosomes appeared after the usual interval in its blood. In order to determine whether the Jinja variety of trypanosomes would develop in the blood of this animal, and thus constitute a difference between it and the “mule” variety, it was injected with blood containing the Jinja variety of trypanosomes. After the incubation period of the latter disease, trypanosomes appeared in the blood of this animal and they continued to be present till its death. The symptoms and duration of the disease were exactly the same as in the Jinja disease; compare Experiment 162.

EXPERIMENT 193. SHEEP.

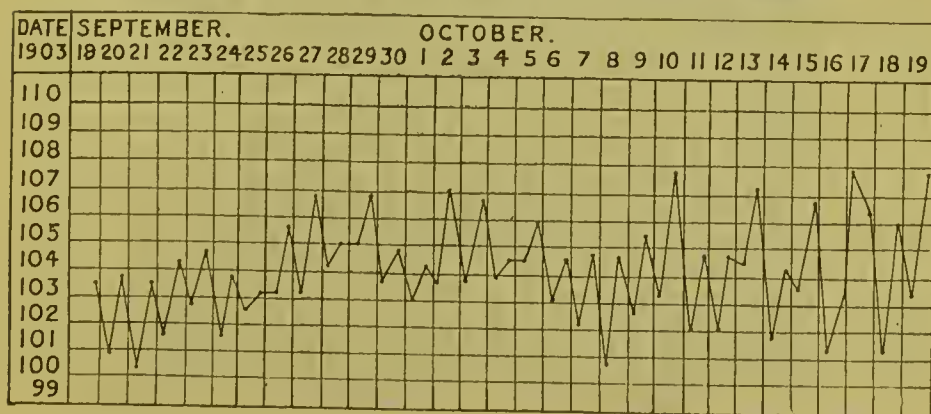
To note the effect of subcutaneous injection of blood from an animal suffering from the “Jinja cattle disease” into a sheep.

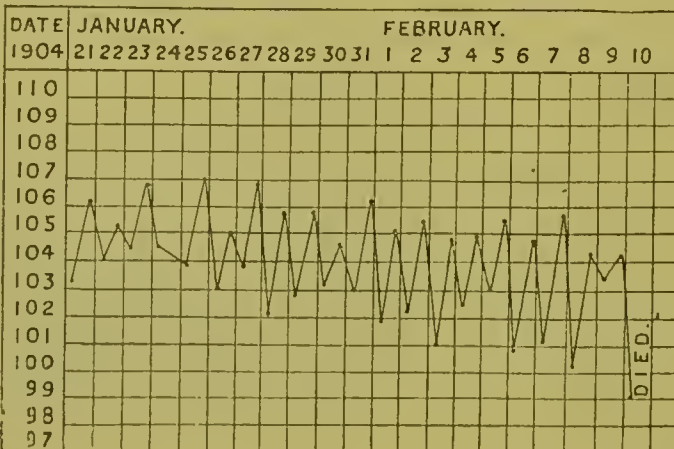
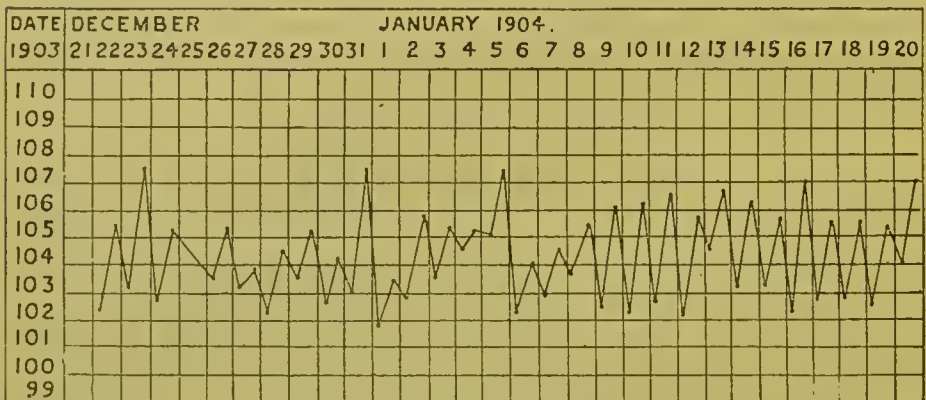
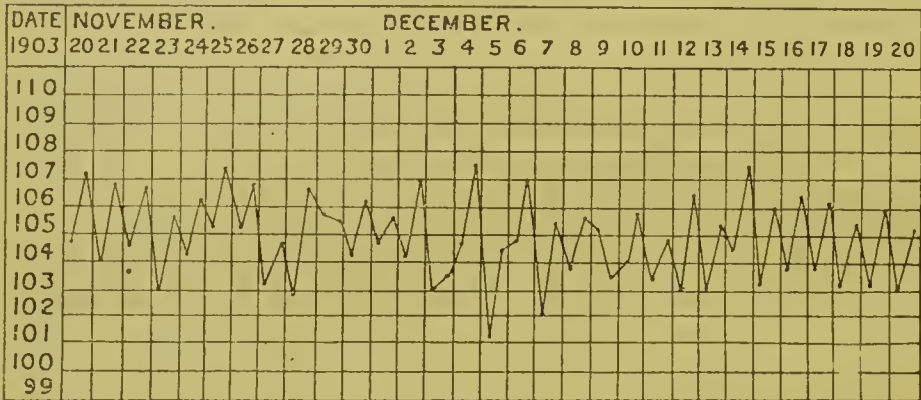
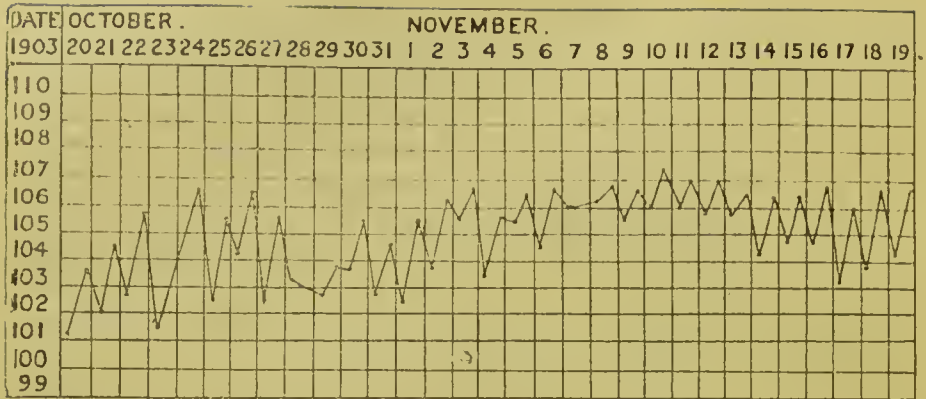
September 25, 1903. Injected subcutaneously 15 e.e. of blood containing active trypanosomes from Monkey 135.

October 13. Many trypanosomes were found in the blood to-day for the first time, eighteen days after inoculation.

February 3, 1904. The animal appears short of breath and is not walking about much. The general state of health is fair.

The following chart shows the course of the disease:—





The following table shows the presence or absence of trypanosomes in the blood:—

Date.				Parasites in the blood.		
				Filaria.	Malaria.	Trypanosoma.
1903.						
Sept.	23	—	—	—
"	30	—
Oct.	3	—
"	7	—
"	10	—
"	11	—
"	13	+
"	16	—
"	17	+
"	19	+
"	21	—
"	27	+
Nov.	4	—
"	11	—
"	18	+
"	25	+
Dec.	2	+
"	9	+
"	16	—
"	23	+
"	30	+
1904.						
Jan.	6	+
"	13	+
"	20	+
"	27	+
Feb.	2	+
"	9	+

February 10. Animal died about 3 p.m. Post-mortem.

There is no marked emaciation. Conjunctivæ pale—slight haziness of corneæ present. There is some increase of pericardial fluid, no increase of fluid in pleural or peritoneal cavities.

Heart.—Well-marked jelly-like material round base.

No endocardial petechiæ. The muscle is very pale. The blood of this organ contained active trypanosomes.

Lungs.—Both are healthy.

Liver.—Nothing noteworthy.

Spleen.—Not enlarged.

Kidneys.—Both pale.

Glands.—In both iliac regions they are enlarged and congested.

Remarks.—This is an interesting experiment, as it clearly demonstrates the course of this disease in a sheep. The animal was not emaciated. It showed no œdema of the sheath or other part. It was only shortly before its death that the animal

showed any abnormal signs, and these were mainly breathlessness and a tendency to lie about.

EXPERIMENT 211. SHEEP.

To note the effect of subcutaneous injection of blood from an animal suffering from the "Abyssinian fly disease" into a sheep.

October 8, 1903. Injected 5 e.e. of blood containing active trypanosomes from Dog 177 into this sheep.

December 2. Again injected 10 e.e. of blood from Dog 256.

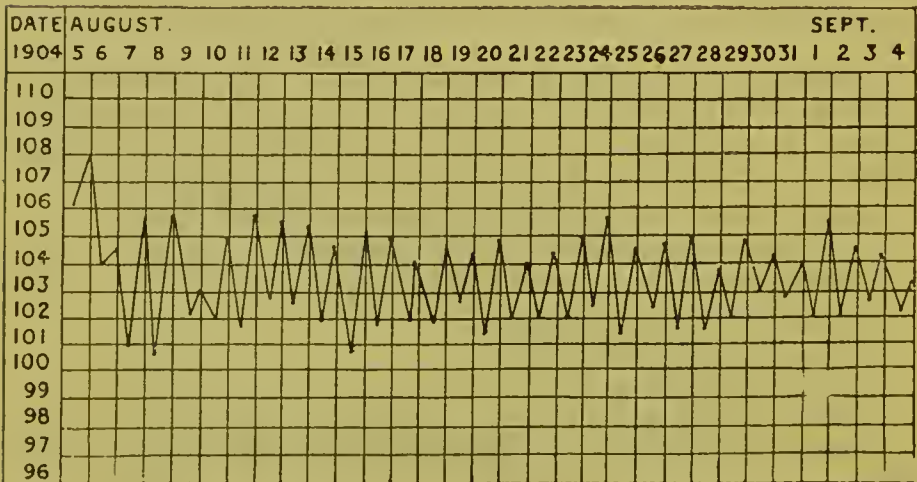
January 13, 1904. This animal keeps in good health and trypanosomes have not appeared in the peripheral blood. The temperature remained normal throughout.

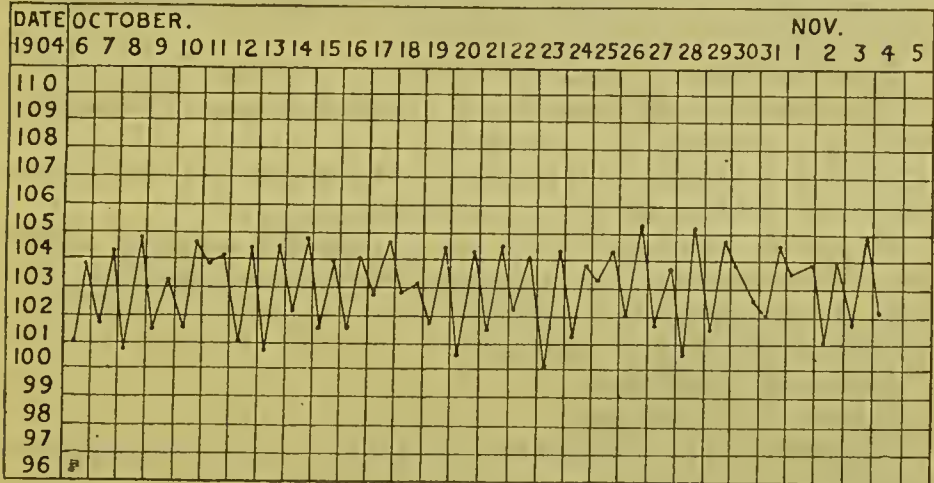
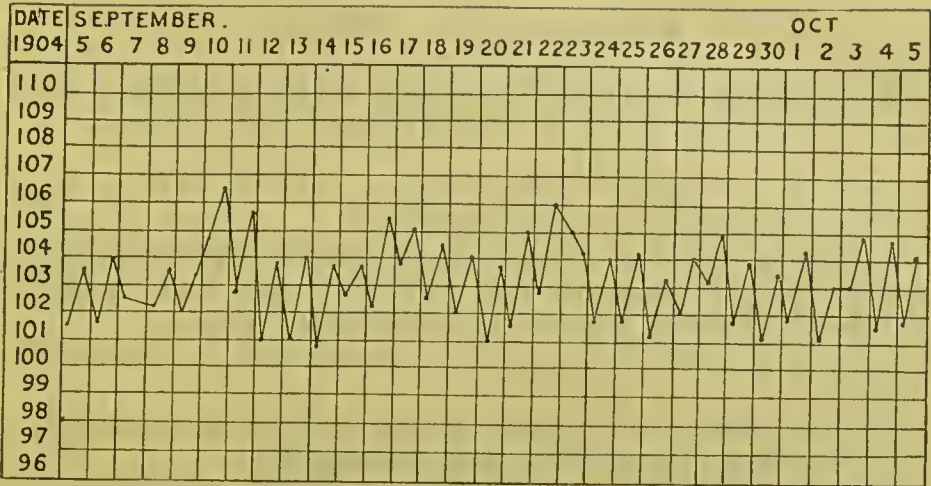
Trypanosomes having failed to appear in the blood, this animal was used "to note effect of subcutaneous injection of blood from an animal suffering from the 'Jinja cattle disease' into a sheep previously inoculated subcutaneously with blood from an animal suffering from 'Abyssinian fly disease,' to which it proved refractory."

August 23, 1904. Eight months after previous injection no trypanosomes having appeared in the blood, 1.5 e.c. of blood from Rabbit 289 was injected subcutaneously into this sheep.

September 28. Trypanosomes appeared in the blood to-day.

The following chart represents the course of the disease:—





The following table shows the presence or absence of trypanosomes in the blood:—

Date.		Parasites in the blood.		
		Filar.	Malar.	Tryp.
1904.				
June	15	—
"	22	—
"	28	—
July	13	—
"	20	—
"	27	—
Aug.	10	—
"	17	—
"	30	—
Sept.	7	—
"	14	—
"	21	—
"	28	+
Oct.	5	+
"	12	—
"	19	+
Nov	2	+

EXPERIMENT 194. SHEEP.

To note the effect of subcutaneous injection of blood from an animal suffering from the "mule disease" into a sheep.

September 28, 1903. Injected 3 c.e. of blood from Monkey No. 180, containing active trypanosomes.

November 8. The trypanosomes not having appeared in the blood of this animal, it was reinjected with 7 c.e. of blood from Jaekal No. 240, containing many trypanosomes.

January 6, 1904. The animal is fat and maintains its health well.

February 9th. The general condition of the animal is good. The temperature remained normal throughout.

The blood was examined weekly, but trypanosomes were never found in the peripheral blood.

June 18. Animal died at 12.30 p.m. Post-mortem.

The body is not emaciated. There are no oedematous swellings. No opacity of corneæ.

There is some increase of fluid in the pericardial cavity; no increase of fluid in pleural or peritoneal cavities.

Heart.—A considerable amount of jelly-like material round base. The muscle is pale, otherwise nothing noteworthy. No active trypanosomes in heart's blood.

Lungs.—Nothing noteworthy.

Liver.—Is congested.

Spleen.—Not enlarged.

Glands in neck enlarged and congested. Juice contains no active trypanosomes.

Remarks.—This experiment is of considerable interest, as it shows the course of this disease in the sheep. As compared with the Jinja disease it runs a very chronic course, and, like the same disease in the Goat 194 and Ox 202, trypanosomes never appeared in the peripheral blood, although the blood of the latter was infective to dogs. There can be little doubt that in the sheep also the result of injection of blood containing this variety of trypanosome is to produce a chronic disease which ultimately kills the animal.

EXPERIMENT 192. GOAT.

To note the effect of subcutaneous injection of blood from an animal suffering from the "Jinja cattle disease" into a goat.

September 25, 1903. Injected subcutaneously 15 c.e. of blood from Monkey 135, containing many trypanosomes, into this goat.

October 8. There was some local reaction at the site of inoculation, but no abscess formation.

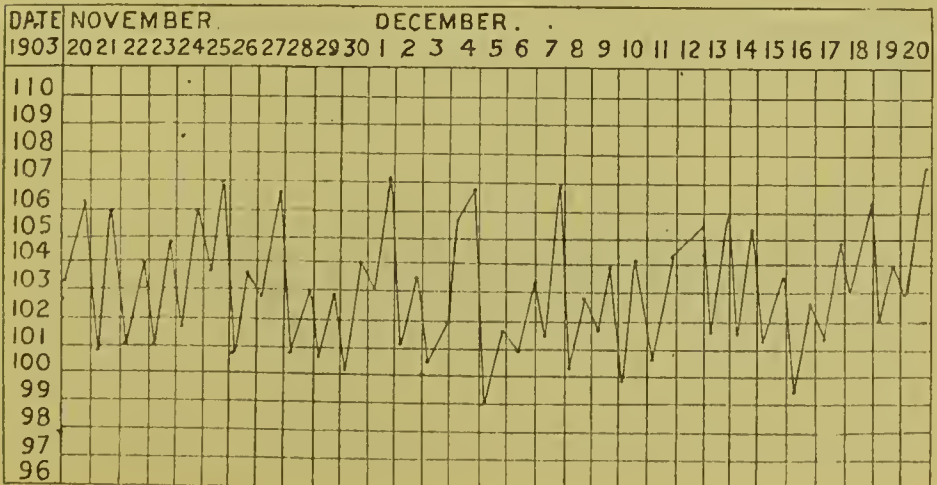
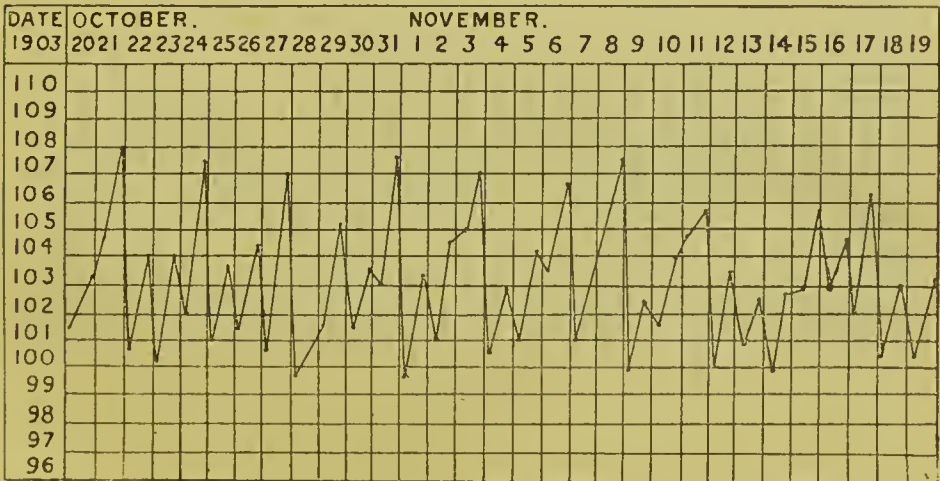
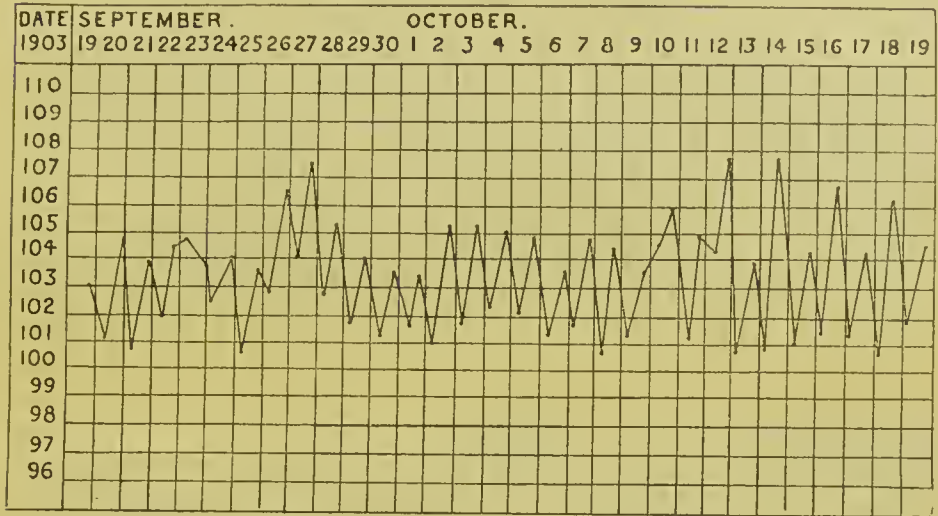
October 10. Trypanosomes appeared in the blood to-day in considerable numbers, the fifteenth day after inoculation.

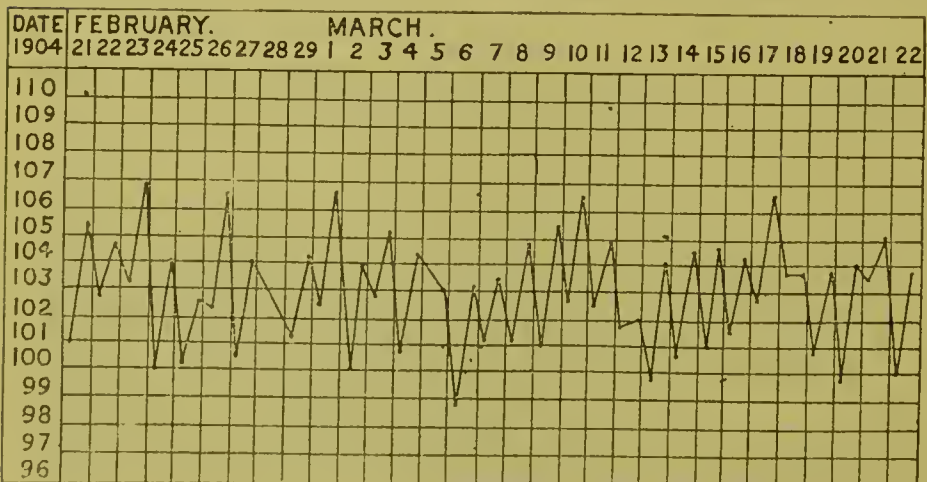
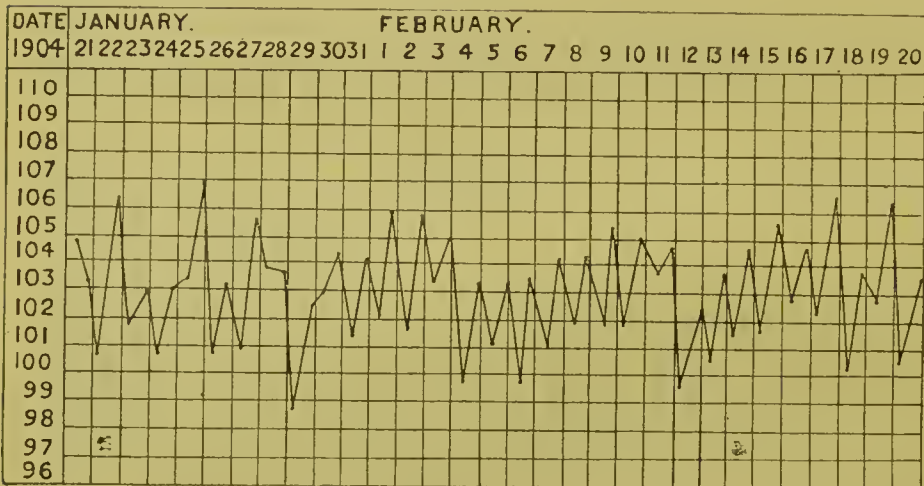
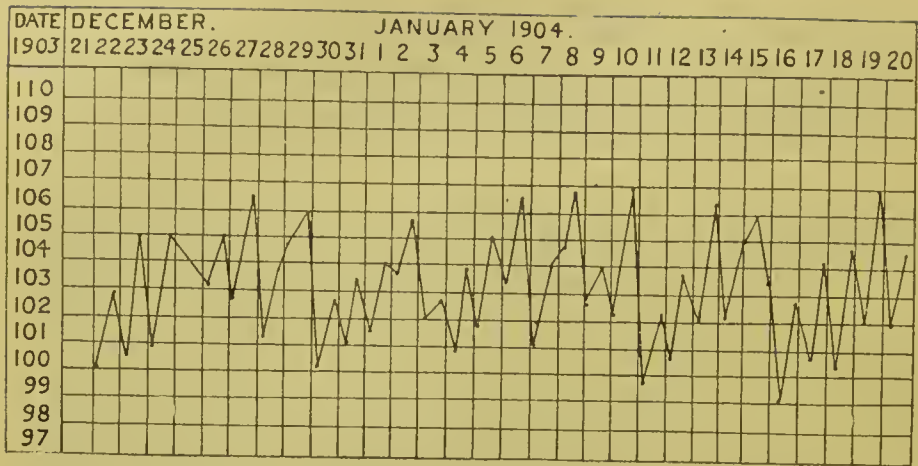
April 27, 1904. An enlarged lymphatic gland was felt in

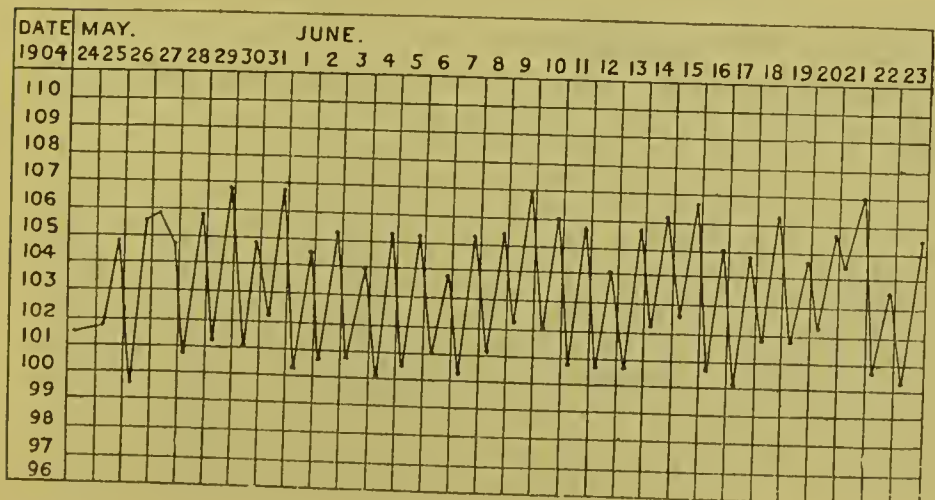
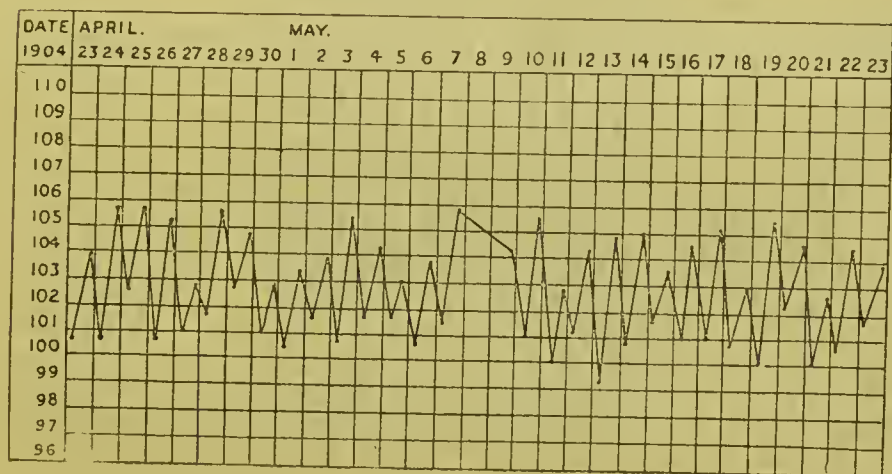
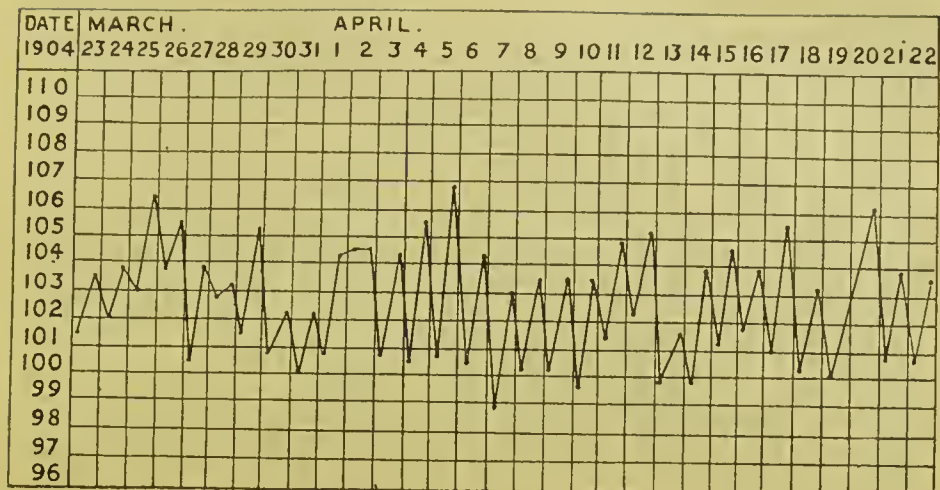
the right supra-clavicular region. This was punctured; the juice showed many active trypanosomes.

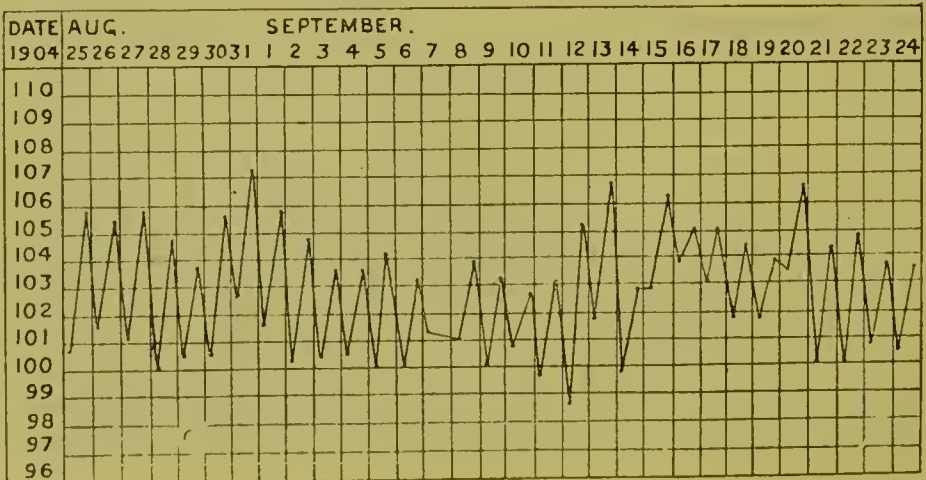
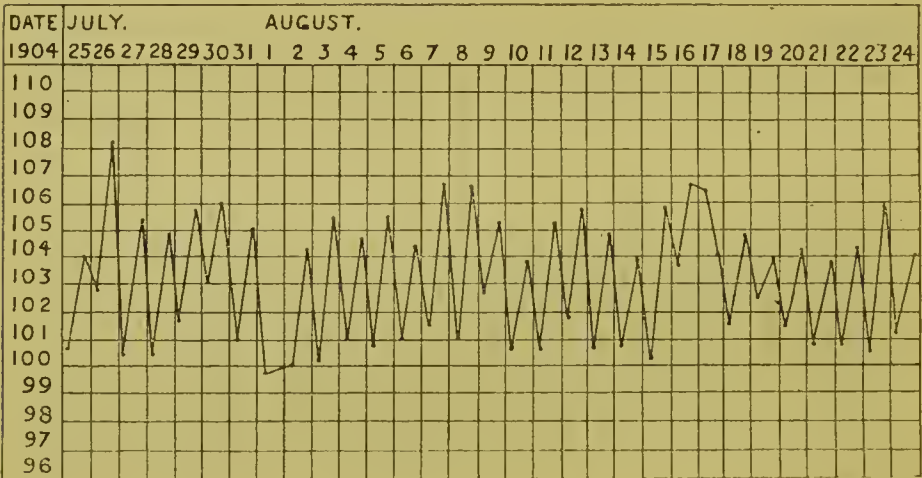
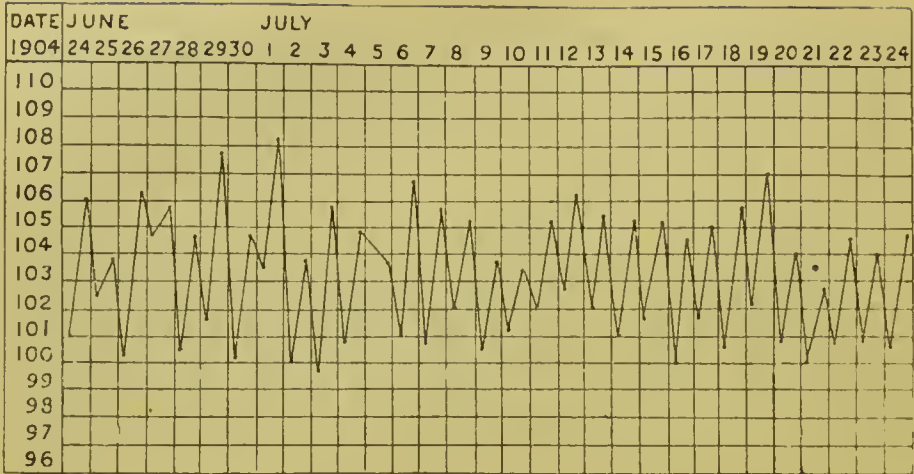
September 27. The animal keeps in good condition. The trypanosomes remain present in the blood.

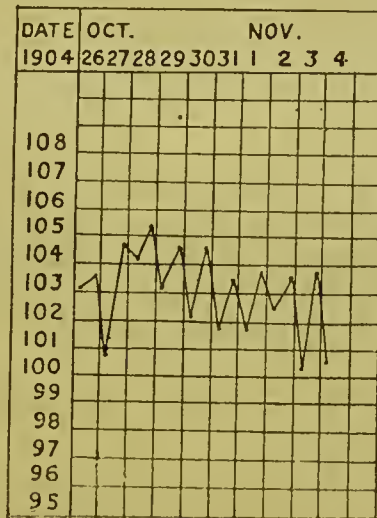
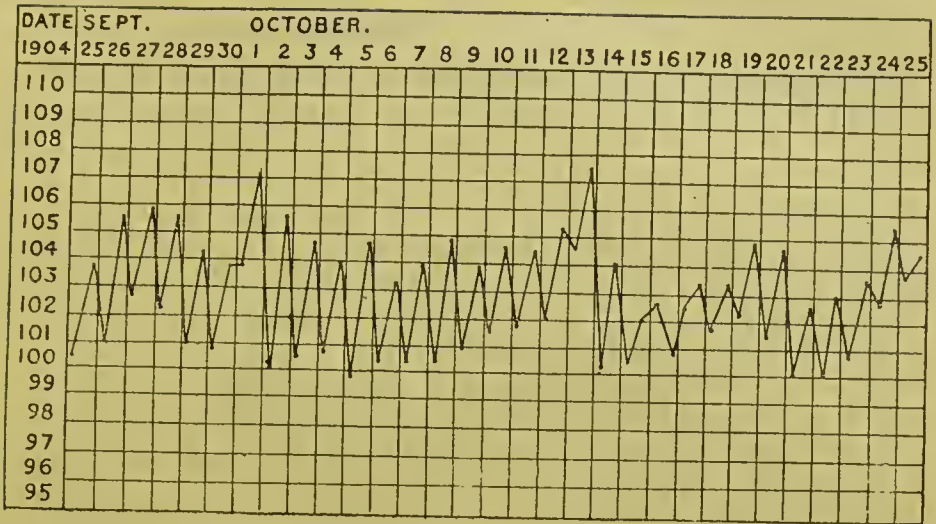
The following chart shows the course of the disease:—











The following table shows the presence or absence of trypanosomes in the blood :—

Date.				Parasites in the blood.		
				Filaria.	Malaria.	Trypanosoma.
Sept.	1903.					
	23	—
	30	—
Oct.	3	—
	7	—
	10	+
	13	+
	16	+
	19	+
	21	+
	28	—

Date.				Parasites in the blood.		
				Filaria.	Malaria.	Trypanosoma.
1903.						
Nov.	4	—
"	11	+
"	18	+
"	25	+
Dec.	2	—
"	9	—
"	16	—
"	23	—
"	30	—
1904.						
Jan.	6	+
"	13	+
"	20	+
"	27	+
Feb.	3	+
"	9	+
"	17	+
"	24	—
March	2	+
"	9	+
"	16	+
"	23	+
"	30	+
April	7	—
"	20	—
"	27	+
May	4	—
"	11	—
"	18	+
"	24	+
June	1	—
"	7	—
"	14	+
"	22	—
"	29	+
July	13	+
"	26	—
Aug.	10	—
"	17	—
"	30	+
Sept.	7	—
"	14	—
"	28	—
Oct.	13	+
"	19	+
Nov.	2	+

Remarks.—This experiment illustrates the very chronic course of this disease in goats. The condition of the animal is good.

EXPERIMENT 212. GOAT.

To note the effect of subcutaneous injection of blood from an animal suffering from the "Abyssinian fly disease" into a goat.

October 8, 1903. Injected subcutaneously 5 c.c. of blood containing active trypanosomes from Dog 177 into this goat.

December 2. Again injected 10 c.c. of blood from Dog 256.

January 13, 1904. The general condition of this animal is good. Trypanosomes have not appeared in the blood.

The temperature remained normal throughout.

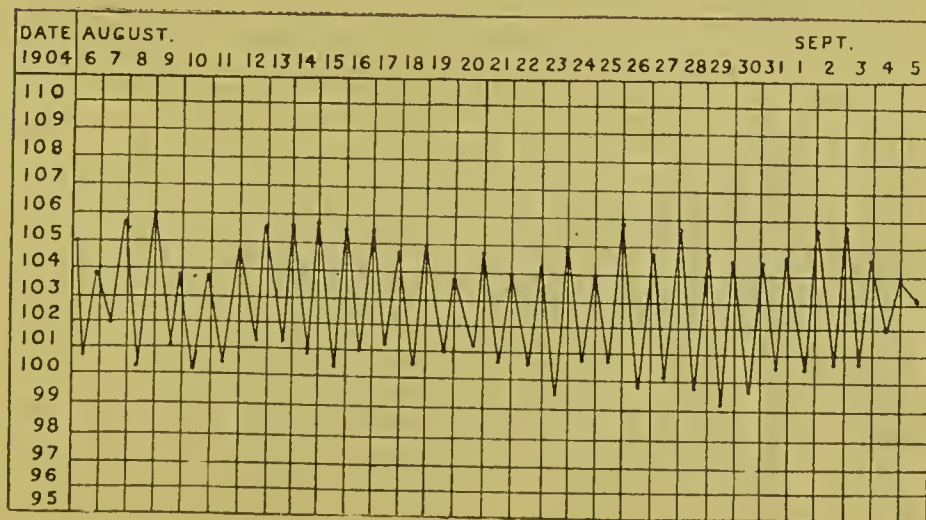
The blood was examined weekly, but no trypanosomes were found in the peripheral circulation at any time.

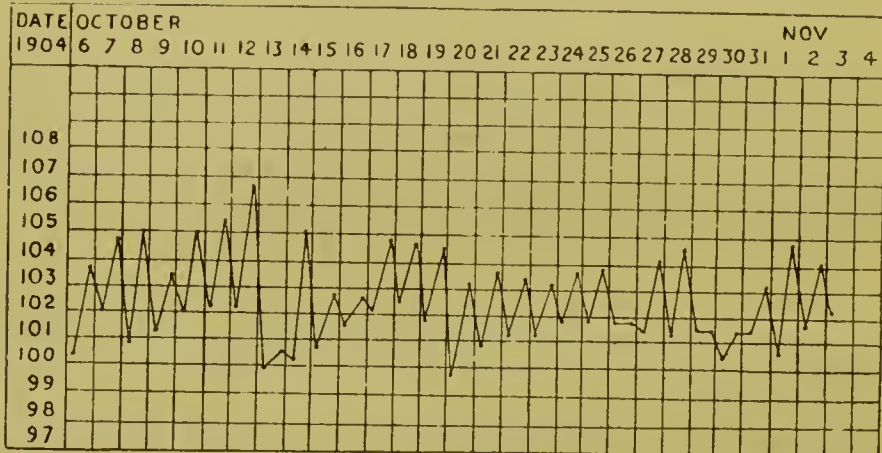
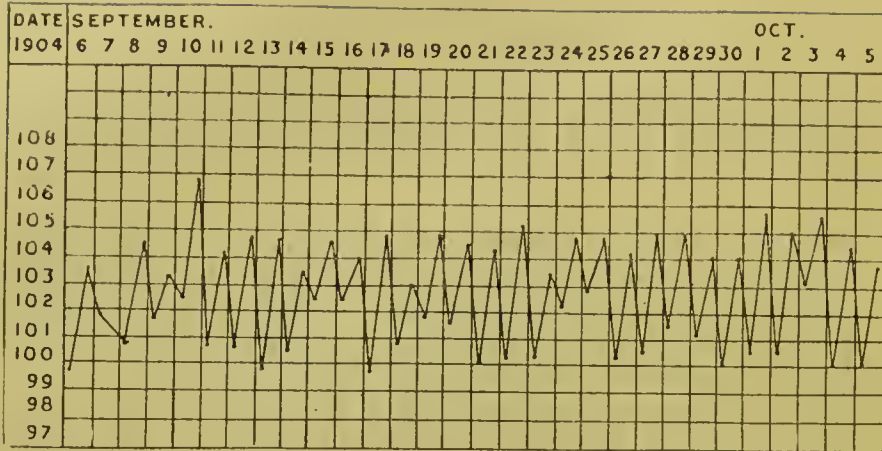
Trypanosomes having failed to appear in the blood, this animal was used "to note the effect of subcutaneous injection of blood from an animal suffering from the 'Jinja cattle disease' into a sheep previously inoculated subcutaneously with blood from an animal suffering from 'Abyssinian fly disease,' to which it proved refractory."

August 23. Eight months after previous injection, no trypanosomes having appeared in the blood, 1.5 c.c. of blood, containing many trypanosomes, from Rabbit 289, was injected subcutaneously.

September 28. Trypanosomes have appeared in the blood to-day.

The following chart represents the course of the disease:—





The following table shows the presence or absence of trypanosomes in the blood :—

				Parasites in the blood.		
Date.				Filaria.	Malaria.	Trypanosoma.
1904.						
June	8	-
"	15	-
"	22	-
"	29	-
July	12	-
"	20	-
"	27	-
August	10	-
"	17	-
"	30	-
Sept.	7	-
"	14	+
"	28	+
Oct.	5	-
"	12	+
"	19	+
Nov.	2	+

EXPERIMENT 194. GOAT.

To note the effects of subcutaneous injection of blood from an animal suffering from "mule cattle disease" into a goat.

September 28, 1903. Injected 3 c.c. of blood containing trypanosomes from a monkey, Experiment 180.

November 8. The trypanosomes have not appeared in the blood of this animal. Reinjecting with 7 c.c. of blood from jaekal, Experiment 240.

The temperature remained normal throughout.

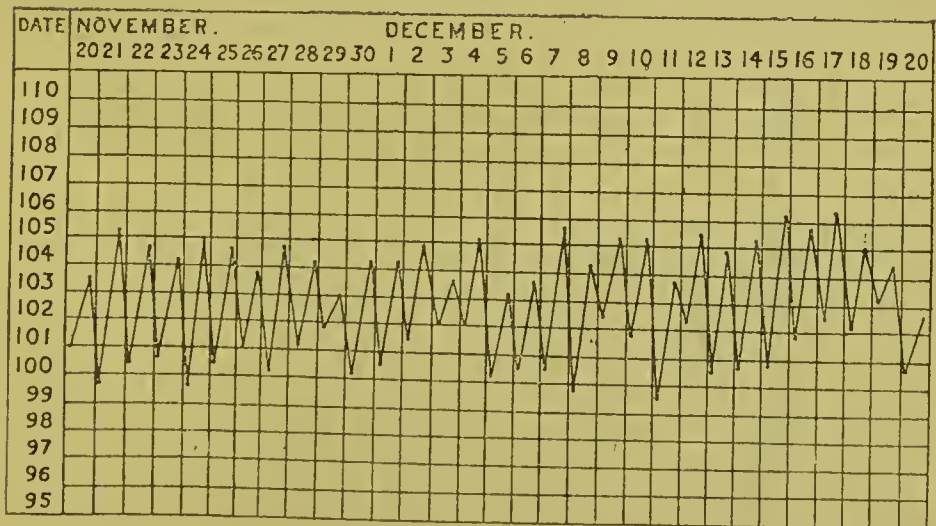
The trypanosomes not having appeared in the blood of this animal, it was used "to note the effect of injection of blood from an animal suffering from the 'Jinja cattle disease' into a goat previously injected with blood containing the 'mule' variety of trypanosome, but which had not appeared in the peripheral blood."

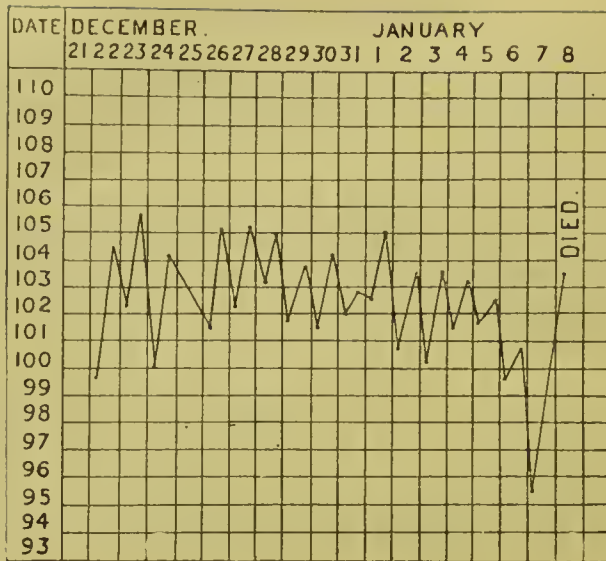
November 21. Injected 10 c.c. of blood subcutaneously from ox, Experiment 162, which was dying.

December 2. The trypanosomes appeared in the blood to-day for the first time, eleven days after inoculation.

January 6, 1904. The animal is pregnant. She appears sick and is lying down.

The following chart shows the course of the disease:—





The following table shows the presence or absence of trypanosomes in the blood:—

Date.				Parasites in the blood.		
				Filaria.	Malaria.	Trypanosoma.
1903.						
Sept.	22	—	—	—
"	30	—
Oct.	3	—
"	6	—
"	10	—
"	13	—
"	16	—
"	19	—
"	21	—
"	26	—
"	28	—
Nov.	2	—
"	4	—
"	11	—
"	18	—
"	25	—
Dec.	2	+
"	9	+
"	16	+
"	23	+
"	30	+
1904.						
Jan.	6	+
"	8	+

January 6. Animal died this morning. Post-mortem.

No emaciation. There is no opacity of the corneæ or oedematous swellings. The superficial glands are slightly

enlarged. No increase of fluid in the pleural, pericardial or peritoneal cavities.

Heart.—A considerable amount of jelly-like material round the base. There are a few petechiæ over right auricle. There are no petechiæ under endocardium. The muscle is pale. The blood of this organ contains trypanosomes.

Lungs.—Both show small extravasations under pleural membrane, otherwise nothing noteworthy.

Liver.—Nothing noteworthy.

Spleen.—Slightly enlarged; substance is soft and friable. Smears from this organ show the presence of trypanosomes.

Kidneys.—Jelly-like substance surrounds both.

Glands.—Along the great vessels they are distinctly enlarged.

Uterus.—Contains two practically full time foetuses. The heart blood of the foetus shows no trypanosomes, nucleated red corpuscles were abundant.

Remarks.—This experiment is an interesting and important one. Its object was to determine firstly the effect of injection of blood containing the "mule variety of trypanosome," and secondly, when this latter failed to appear in the blood, to determine whether the "Jinja cattle" trypanosome would develop in the blood of the same animal. The first injection was not followed by the appearance of trypanosomes in the blood, although two inoculations were performed, but when the blood containing the "Jinja variety" of trypanosome was injected the parasites appeared in the blood after the usual incubation period for this disease and continued to be present until the death. The death was due to the trypanosomes, perhaps hastened by the pregnancy. The above experiment suggests that as regards their action in goats there is a difference between the trypanosomes of the "mule" and the "Jinja cattle."

16. *Are we dealing with one or more than one species of Trypanosoma?*

As has been shown the *Trypanosoma gambiense* differs in morphological characters from the animal varieties studied here. The difference is more marked in their behaviour when inoculated into the various experimental animals. From a consideration of the results obtained, the first conclusion that will be arrived at is that the trypanosomes found in the animals in Uganda are different from those found in sleeping sickness cases, and in men showing no signs of sleeping sickness, the two latter trypanosomes being identical, being in fact the *Trypanosoma gambiense* of the West Coast. As to the nature of the animal trypanosomes, the facts may be summed up as follows:—The trypanosoma of Mr. Pordage's ox when inoculated into a monkey and dog failed to appear in the blood of either; it further appeared and developed in the blood of an ox. In these results a difference is established

between this variety of trypanosoma and the *Trypanosoma gambiense*. Owing to the fact that it did not take in the experimental animals, it was not possible to study this "strain" so fully as the others.

With regard to the other varieties it will be at once obvious that the Jinja trypanosoma marks itself off from the other two in its behaviour when inoculated into animals. It runs a more acute course, and is capable of developing in all the experimental animals except the baboon, whilst the Abyssinian and mule do not develop in the blood of sheep, oxen and goats. Thus a distinct difference is constituted between the Jinja trypanosoma on the one hand and the Abyssinian and the mule on the other. This was also established by inoculating animals resistant to the two latter varieties of trypanosoma with the Jinja "strain."

The reactions in animals of the trypanosoma found in the mule at Entebbe and that obtained from the Abyssinian boundary are in all respects similar. The Jinja trypanosoma most closely approaches the classical African type (Nagana), and is, probably, identical with it. The other two differ from this type, and may be provisionally included under the unclassified varieties of African trypanosomes. It may be briefly stated that the species of trypanosomes which have been met with here are: (1) *Trypanosoma gambiense*, which is identical with those found in sleeping sickness cases and in cases of so-called "*Trypanosoma fever*"; (2) *Trypanosoma brucei* or a very closely related species, with which the Jinja cattle trypanosoma is identical; (3) a trypanosoma which occasioned the death of mules in Abyssinia and a mule in Uganda, and which is provisionally unclassified; (4) the trypanosoma of Mr. Pordage's ox.

The following table shows the result of the injection of the various animals with the different "strains" of trypanosomes:—

Table showing the results of injection of the various trypanosomes found in Uganda into different animals.

Animals used for experiment.	Presence or absence of trypanosomes in the blood after inoculation with fluids containing trypanosomes from						
	Sleeping sickness cases.	Men having no marked signs of sleeping sickness.	Fresh flies, Entebbe.	Mr. Portage's ox.	Jinja cattle.	Abyssinian animals.	Mule, Entebbe.
1. Monkeys—							
<i>a.</i> Cercopithecus sp.	...						
<i>b.</i> Macacus Rhesus	+	+	+	—	+	+	+
2. Dogs—							
<i>a.</i> Adult	...	+
<i>b.</i> Pup	+	—	+	—	+	+	+
3. Jackals	...	+
4. Cats—							
<i>a.</i> Adult	+	+
<i>b.</i> Kitten	+	+
5. Rats...	+	+
6. Rabbits	+	+	+
7. Guinea pigs...	+	+	+
8. Sheep	...	+	+	+	+
9. Goats	...	—	+	—	—
10. Oxen	...	—	+	—	—
11. Masai donkey	...	—	+	—	—
12. Dog-faced baboons	+	+	+
13. Mule	—

TABLE SHOWING RESULT OF INOCULATION OF ANIMALS IMMUNE TO ONE VARIETY OF TRYPANOSOMA, WITH ANOTHER STRAIN:—

No. of Experiment.	Variety of Trypanosoma to which animal is immune.	Variety of Trypanosoma used for inoculation.	Date of Inoculation.	Result of Inoculation.	Remarks.
Ox 202 ...	Mule ...	Jinja ...	Nov. 21, 1903	Trypanosomes appeared in the blood on the 12th day. Died 20.1.04.	Rise of temperature after inoculation.
Goat 194...	" ...	" ...	" "	Trypanosomes appeared in the blood on the 12th day. Died 20.1.04.
Sheep 191	" ...	" ...	Control	...	Trypanosomes have never appeared in the blood.
Sheep 211	Abyssinian ...	" ...	Aug. 23, 1904	Trypanosomes appeared in the blood 36 days after inoculation.	Still alive.
Goat 212	" ...	" ...	" "	Trypanosomes appeared in the blood 36 days after inoculation.	Still alive.
Ox 209 ...	" ...	" ...	Control	...	Trypanosomes have never appeared in the blood.

17. *Can the Glossina palpalis convey the Trypanosoma found in the Jinja Cattle, Entebbe and Abyssinian Mules to Healthy Animals?*

The animal employed for these experiments was the monkey. The dog is quite unsuitable owing to the difficulty, already mentioned, of obtaining an animal free from anchylostomes. The method employed was to feed tsetse flies on an animal suffering from the above diseases and then, after varying intervals of time, to place the same cage of flies on a healthy monkey. Only the flies which had filled themselves were counted as having fed:—

EXPERIMENT 196. MONKEY (*Cercopithecus sp.*).

Feeding tsetse flies (*Glossina palpalis*) on a healthy monkey 6 hours after they had been fed on a monkey infected with the "Jinja cattle disease."

Date.	Number of flies fed on :—		Tryp.	Date.	Number of flies fed on :—		Tryp.
	Infected Monkey.	Healthy Monkey.			Infected Monkey.	Healthy Monkey.	
1903.				1903.			
Sept. 22...	Absent.	Oct. 8...	11	8	...
" 23...	10	11	...	" 9...	9	13	...
" 24...	7	13	...	" 10...	11	14	Absent.
" 25...	16	14	Absent.	" 11...	14	16	...
" 26...	15	14	...	" 12...	7	12	...
" 27...	10	17	...	" 13...	6	12	...
" 28...	20	12	...	" 14...	12	10	...
" 29...	14	9	...	" 15...	10	8	...
" 30...	12	10	...	" 16...	12	14	...
Oct. 1...	16	12	...	" 17...	10	9	Present.
" 2...	12	11	...	" 18...
" 3...	13	8	Absent.	" 19...
" 4...	14	9	...	" 20...
" 5...	10	9	...	" 21...
" 6...	18	11	...	" 22...
" 7...	9	10

EXPERIMENT 204. MONKEY (*Cercopithecus sp.*).

Feeding flies (*Glossina palpalis*) on a healthy monkey 24 hours after they had been fed on a monkey infected with the trypanosomes of the "Jinja cattle disease."

Number of flies fed on :—				Number of flies fed on :—			
Date.			Tryp.	Date.			Tryp.
	Infected Monkey.	Healthy Monkey.			Infected Monkey.	Healthy Monkey.	
1903.				1903.			
Sept. 27...	...	14	Absent.	Nov. 19...	4	...	Absent.
" 28...	17	" 20...	...	6	...
" 29...	...	24	...	" 21...	8
" 30...	26	" 22...	...	0	...
Oct. 1...	...	12	...	" 23...	13
" 2...	14	" 24...	...	0	...
" 3...	" 25...	4
" 4...	5	" 26...	...	8	Absent.
" 5...	...	16	Absent.	" 27...	7
" 6...	14	" 28...	...	10	...
" 7...	...	9	...	" 29...	6
" 8...	9	" 30...	...	8	...
" 9...	...	16	...	Dec. 1...	10
" 10...	12	...	Absent.	" 2...	...	12	...
" 11...	...	12	...	" 3...	10	...	Absent.
" 12...	14	" 4...	...	6	...
" 13...	...	9	...	" 5...	8
" 14...	40	" 6...	...	4	...
" 15...	...	14	...	" 7...	6
" 16...	24	" 8...	...	3	...
" 17...	...	26	Absent.	" 9...	6
" 18...	12	" 10...	...	5	Absent.
" 19...	...	16	...	" 11...	8
" 20...	9	" 12...	...	0	...
" 21...	...	20	...	" 13...	3
" 22...	8	...	Absent.	" 14...	...	6	...
" 23...	...	18	...	" 15...	6
" 24...	10	" 16...	...	7	...
" 25...	...	16	...	" 17...	3	...	Absent.
" 26...	12	" 18...	...	4	...
" 27...	...	8	...	" 19...	4
" 28...	11	" 20...	...	3	...
" 29...	...	0	Absent.	" 21...	5
" 30...	14	" 22...	...	2	...
" 31...	...	14	...	" 23...	5
Nov. 1...	16	" 24...	...	3	Absent.
" 2...	...	5	...	" 25...	0
" 3...	10	" 26...	...	7	...
" 4...	...	14	Absent.	" 27...	12
" 5...	8	" 28...	...	2	...
" 6...	...	12	...	" 29...	15
" 7...	5	" 30...	...	19	...
" 8...	...	0	...	" 31...	12	...	Absent.
" 9...	4				
" 10...	...	0	...	1904.			
" 11...	20	Jan. 1...	...	12	...
" 12...	...	10	Absent.	" 2...	10
" 13...	8	" 3...	...	0	...
" 14...	...	12	...	" 4...	10
" 15...	14	" 5...	...	6	...
" 16...	...	6	...	" 6...	13
" 17...	7	" 7...	...	5	Absent.
" 18...	...	8	...	" 8...	15

Date.	Number of flies fed on :—		Tryp.	Date.	Number of flies fed on :—		Tryp.
	Infected Monkey.	Healthy Monkey.			Infected Monkey.	Healthy Monkey.	
1904.				1904.			
Jan. 9...	...	10	...	Jan. 19...	...	12	...
" 10...	9	" 20...	8
" 11...	...	7	...	" 21...	...	4	Absent.
" 12...	12	" 22...	14
" 13...	...	0	...	" 23...	...	8	...
" 14...	7	...	Absent.	" 24...	6
" 15...	...	12	...	" 25...	...	7	...
" 16...	6	" 26...	10
" 17...	...	9	...	" 27...	...	3	...
" 18...	5	" 28...	4	...	Present.

EXPERIMENT 199. MONKEY (*Cercopithecus sp.*).

Feeding tsetse flies (*Glossina palpalis*) on a healthy monkey 6 hours after they had been fed on a monkey infected with the trypanosome of the "Abyssinian fly disease."

Date.	Number of flies fed on :—		Tryp.	Date.	Number of flies fed on :—		Tryp.
	Infected Monkey.	Healthy Monkey.			Infected Monkey.	Healthy Monkey.	
1903.				1903.			
Sept. 26	14	10	Absent.	Oct. 18	9	7	...
" 27	11	14	...	" 19	8	12	...
" 28	8	3	...	" 20	12	9	...
" 29	20	13	...	" 21	10	11	...
" 30	27	11	...	" 22	12	14	...
Oct. 1	8	9	...	" 23	11	17	Absent.
" 2	8	6	...	" 24	10	9	...
" 3	6	9	Absent.	" 25	8	26	...
" 4	11	7	...	" 26	12	10	...
" 5	14	8	...	" 27	10	13	...
" 6	20	12	...	" 28	18	14	...
" 7	11	17	...	" 29	20	12	Absent.
" 8	9	14	...	" 30	18	14	...
" 9	6	20	...	" 31	20	12	...
" 10	10	13	Absent.	Nov. 1	18	12	...
" 11	11	9	...	" 2	12	14	...
" 12	14	10	...	" 3	14	12	...
" 13	16	11	...	" 4	12	10	...
" 14	14	18	...	" 5	14	16	Absent.
" 15	21	8	...	" 6	16	10	...
" 16	14	18	...	" 7	14	0	...
" 17	12	14	Absent.	" 8	16	18	...

Date.	Number of flies fed on :—		Tryp.	Date.	Number of flies fed on :—		Tryp.
	Infected Monkey.	Healthy Monkey.			Infected Monkey.	Healthy Monkey.	
1903.				1904.			
Nov. 9	14	12	...	Jan. 1	6	6	...
" 10	12	14	...	" 2	4	11	...
" 11	10	16	...	" 3	19	6	...
" 12	12	14	Absent.	" 4	22	10	...
" 13	10	8	...	" 5	10	6	...
" 14	8	12	...	" 6	5	12	...
" 15	7	10	...	" 7	5	6	Absent.
" 16	12	10	...	" 8	12	5	...
" 17	9	9	...	" 9	8	12	...
" 18	10	10	...	" 10	12	10	...
" 19	12	16	Absent.	" 11	10	7	...
" 20	14	15	...	" 12	6	5	...
" 21	9	8	...	" 13	10	7	...
" 22	7	8	...	" 14	5	7	Absent.
" 23	6	14	...	" 15	10	6	...
" 24	12	11	...	" 16	14	10	...
" 25	14	4	...	" 17	6	7	...
" 26	12	14	Absent.	" 18	8	7	...
" 27	14	8	...	" 19	5	7	...
" 28	14	10	...	" 20	6	5	...
" 29	16	14	...	" 21	4	6	Absent.
" 30	12	3	...	" 22	8	6	...
Dec. 1	10	12	...	" 23	8	6	...
" 2	12	10	...	" 24	2	8	...
" 3	10	6	Absent.	" 25	3	6	...
" 4	8	10	...	" 26	2	8	...
" 5	10	7	...	" 27	4	4	...
" 6	8	6	...	" 28	3	4	Absent.
" 7	12	6	...	" 29	2	6	...
" 8	10	6	...	" 30	4	5	...
" 9	8	6	...	" 31	2	5	...
" 10	10	8	Absent.	Feb. 1	0	3	...
" 11	9	11	...	" 2	3	8	...
" 12	8	8	...	" 3	2	3	...
" 13	5	7	...	" 4	5	7	Absent.
" 14	8	8	...	" 5	6	16	...
" 15	6	8	...	" 6	3	10	...
" 16	8	8	...	" 7	14	12	...
" 17	6	4	Absent.	" 8	10	5	...
" 18	5	6	...	" 9	10	8	...
" 19	10	5	...	" 10	10	8	...
" 20	4	5	...	" 11	18	18	Absent.
" 21	3	7	...	" 12	4	6	...
" 22	4	6	...	" 13	5	9	...
" 23	3	6	...	" 14	5	7	...
" 24	6	5	Absent.	" 15	18	14	...
" 25	0	0	...	" 16	6	8	...
" 26	6	3	...	" 17	5	9	...
" 27	8	5	...	" 18	4	7	Absent.
" 28	9	3	...	" 19	4	4	...
" 29	4	2	...	" 20	4	4	...
" 30	5	3	...	" 21	6	2	...
" 31	10	5	Absent.	" 22	4	6	...

Date.	Number of flies fed on :—		Tryp.	Date.	Number of flies fed on :—		Tryp.
	Infected Monkey.	Healthy Monkey.			Infected Monkey.	Healthy Monkey.	
1904.				1904 ¹			
Feb. 23	6	4	...	March 3	4	6	...
" 24	8	10	...	" 4	4	6	Absent.
" 25	4	5	Absent.	" 5	6	6	...
" 26	6	8	...	" 6	6	4	...
" 27	5	4	...	" 7	5	3	...
" 28	5	4	...	" 8	3	8	...
" 29	3	4	...	" 9	4	4	...
March 1	6	8	...	" 10	4	4	...
" 2	2	8	...	" 11	4	5	Present.

EXPERIMENT 252. MONKEY (*Cercopithecus sp.*).

Feeding flies (*Glossina palpalis*) on a healthy monkey 24 hours after they had been fed on a monkey infected with the "Abyssinian fly disease."

Date.	Number of flies fed on :—		Tryp.	Date.	Number of flies fed on :—		Tryp.
	Infected Monkey.	Healthy Monkey.			Infected Monkey.	Healthy Monkey.	
1903.				1903.			
Nov. 14...	Dec. 7...	...	7	...
" 15...	...	12	...	" 8...	11
" 16...	10	" 9...	...	0	...
" 17...	...	8	...	" 10...	0	...	Absent.
" 18...	10	" 11...	...	12	...
" 19...	...	5	Absent.	" 12...	12
" 20...	0	" 13...	...	5	...
" 21...	...	12	...	" 14...	8
" 22...	4	" 15...	...	8	...
" 23...	...	18	...	" 16...	6
" 24...	14	" 17...	...	5	Absent.
" 25...	...	9	Absent.	" 18...	0
" 26...	8	" 19...	...	5	...
" 27...	...	14	...	" 20...	5
" 28...	14	" 21...	...	5	...
" 29...	...	24	...	" 22...	5
" 30...	16	" 23...	...	6	...
Dec. 1...	...	7	...	" 24...	6
" 2...	10	" 25...	...	0	...
" 3...	...	12	Absent.	" 26...	10
" 4...	7	" 27...	...	8	...
" 5...	...	9	...	" 28...	6
" 6...	5	" 29...	...	5	...

Date.	Number of flies fed on :—		Tryp.	Date.	Number of flies fed on :—		Tryp.
	Infected Monkey.	Healthy Monkey.			Infected Monkey.	Healthy Monkey.	
1903.				1904.			
Dec. 30...	8	Jan. 18...	...	4	...
" 31...	...	6	Absent.	" 19...	7
1904.				" 20...	...	4	...
Jan. 1...	4	" 21...	5	...	Absent.
" 2...	...	5	...	" 22...	...	8	...
" 3...	6	" 23...	24
" 4...	...	5	...	" 24...	...	16	...
" 5...	3	" 25...	0
" 6...	...	3	...	" 26...	...	10	...
" 7...	10	...	Absent.	" 27...	0
" 8...	...	4	...	" 28...	...	14	...
" 9...	8	" 29...	2	...	Absent.
" 10...	...	15	...	" 30...	...	12	...
" 11...	4	" 31...	2
" 12...	...	4	...	Feb. 1...	...	4	...
" 13...	12	" 2...	4
" 14...	...	8	...	" 3...	...	6	...
" 15...	4	" 4...	Present.
" 16...	...	5	...	" 5...
" 17...	5	" 6...

EXPERIMENT 203. MONKEY (*Cercopithecus sp.*).

Feeding flies (*Glossina palpalis*) on a healthy monkey 24 hours after they had been fed on a monkey infected with the trypanosomes of the "mule disease."

Date.	Number of flies fed on :—		Tryp.	Date.	Number of flies fed on :—		Tryp.
	Infected Monkey.	Healthy Monkey.			Infected Monkey.	Healthy Monkey.	
1903.				1903.			
Sept. 27...	10	...	Absent.	Oct. 14...	...	11	...
" 28...	...	10	...	" 15...	5
" 29...	14	" 16...	...	8	...
" 30...	...	9	...	" 17...	5	...	Absent.
Oct. 1...	10	" 18...	...	4	...
" 2...	...	9	...	" 19...	9
" 3...	11	...	Absent.	" 20...	...	8	...
" 4...	...	14	...	" 21...	10
" 5...	11	...	Absent.	" 22...	...	7	Absent.
" 6...	...	6	...	" 23...
" 7...	7	" 24...
" 8...	...	14	...	" 25...	20
" 9...	14	" 26...	...	14	...
" 10...	...	7	Absent.	" 27...	14
" 11...	9	" 28...	...	11	...
" 12...	...	9	...	" 29...	18	...	Present.
" 13...	7	" 30...	...	10	...

18. *Can other biting Flies (Stomoxys) convey the Trypanosoma found in the Jinja Cattle, Entebbe and Abyssinia Mules to Healthy Animals ?*

Exactly similar experiments to the above were carried out, the only difference being that instead of *Glossina palpalis* another common biting fly met with in Uganda (*Stomoxys*) was used, these experiments are given in full:—

EXPERIMENT 223. MONKEY (*Cercopithecus sp.*).

Feeding biting flies (*Stomoxys*) on a healthy monkey which had been fed 8 hours before on a monkey infected with the trypanosomes of the "Jinja cattle disease."

Date.	Number of flies fed on :—		Tryp.	Date.	Number of flies fed on :—		Tryp.
	Infected Monkey.	Healthy Monkey.			Infected Monkey.	Healthy Monkey.	
1903.				1903.			
Oct. 11...	7	8	...	Nov. 15...	12	16	...
" 12...	24	18	Absent.	" 16...	16	13	...
" 13 ..	12	22	...	" 17...	10	18	...
" 14...	8	10	...	" 18...	12	26	...
" 15...	14	16	...	" 19...	18	12	Absent.
" 16...	16	24	...	" 20...	16	14	...
" 17...	14	16	...	" 21...	14	12	...
" 18...	20	18	...	" 22...	10	12	...
" 19...	14	17	Absent.	" 23...	14	22	...
" 20...	18	15	...	" 24...	11	10	...
" 21...	18	18	...	" 25...	14	12	...
" 22...	14	12	Absent.	" 26...	14	0	Absent.
" 23...	19	14	...	" 27...	10	12	...
" 24...	0	0	...	" 28...	14	30	...
" 25...	0	0	...	" 29...	18	20	...
" 26...	7	6	...	" 30...	10	11	...
" 27...	8	6	...	Dec. 1...	12	14	...
" 28...	7	10	...	" 2... 14	9
" 29...	8	9	Absent.	" 3... 14	15	Absent.	Absent.
" 30...	12	10	...	" 4... 16	18
" 31...	14	10	...	" 5... 11	16
Nov. 1...	12	14	...	" 6... 12	18
" 2...	12	16	...	" 7... 14	25
" 3...	10	12	...	" 8... 15	16
" 4...	8	14	...	" 9... 12	6
" 5...	12	17	Absent.	" 10... 14	12	Absent.	Absent.
" 6...	14	18	...	" 11... 12	14
" 7...	10	0	...	" 12... 10	12
" 8...	14	16	...	" 13... 7	12
" 9...	12	12	...	" 14... 12	10
" 10...	10	14	...	" 15... 7	22
" 11...	18	14	...	" 16... 16	14
" 12...	14	10	Absent.	" 17... 12	16	Absent.	Absent.
" 13...	8	14	...	" 18... 10	16
" 14...	6	12	...	" 19... 12	10

Date.	Number of flies fed on :--		Tryp.	Date.	Number of flies fed on :--		Tryp.
	Infected Monkey.	Healthy Monkey.			Infected Monkey.	Healthy Monkey.	
1903.				1904.			
Dec. 20...	7	14	...	Jan. 30...	6	8	...
" 21...	24	16	...	" 31...	5	4	...
" 22...	14	20	...	Feb. 1...	4	6	...
" 23...	8	12	...	" 2...	6	4	...
" 24...	12	10	Absent.	" 3...	4	8	...
" 25...	...	5	...	" 4...	4	8	Absent.
" 26...	10	4	...	" 5...	11	12	...
" 27...	12	14	...	" 6...	8	6	...
" 28...	12	25	...	" 7...	5	6	...
" 29...	9	12	...	" 8...	6	8	...
" 30...	7	28	...	" 9...	16	12	...
" 31...	12	20	Absent.	" 10...	12	10	...
1904.				" 11...	10	6	Absent.
Jan. 1...	10	20	...	" 12...	8	8	...
" 2...	12	6	...	" 13...	8	4	...
" 3...	5	13	...	" 14...	10	15	...
" 4...	6	10	...	" 15...	0	0	...
" 5...	8	10	...	" 16...	0	0	...
" 6...	18	15	...	" 17...	0	0	Absen
" 7...	10	10	Absent.	" 18...	...	9	...
" 8...	10	8	...	" 19...	...	4	...
" 9...	5	16	...	" 20...	4	2	...
" 10...	9	6	...	" 21...	6	6	...
" 11...	15	15	...	" 22...	8	10	...
" 12...	12	8	...	" 23...	10	10	...
" 13...	18	4	...	" 24...	9	6	...
" 14...	6	13	Absent.	" 25...	5	3	Absent.
" 15...	6	5	...	" 26...	5	4	...
" 16...	10	8	...	" 27...	4	2	...
" 17...	5	26	...	" 28...	6	14	...
" 18...	6	24	...	" 29...	8	6	...
" 19...	8	10	...	Mar. 1...	9	8	...
" 20...	7	6	...	" 2...	5	4	...
" 21...	5	7	Absent	" 3...	4	4	...
" 22...	6	4	...	" 4...	3	3	Absent.
" 23...	5	7	...	" 5...	6	6	...
" 24...	3	4	...	" 6...	5	4	...
" 25...	4	6	...	" 7...	4	3	...
" 26...	5	5	...	" 8...	3	2	...
" 27...	6	4	...	" 9...	6	5	...
" 28...	10	3	Absent.	" 10...	8	5	...
" 29...	5	5	...	" 11...	3	6	Absent.
				" 12...	...	4	Stopped.

EXPERIMENT 254. MONKEY (*Cercopithecus* sp.).

Feeding biting flies (*Stomoxys*) on a healthy monkey which had been fed 24 hours previously on a monkey infected with the trypanosomes of the "Jinja cattle disease."

Date.	Number of flies fed on :—		Tryp.	Date.	Number of flies fed on :—		Tryp.
	Infected Monkey.	Healthy Monkey.			Infected Monkey.	Healthy Monkey.	
1903.				1904.			
Nov. 19...	Absent.	Jan. 13...	...	13	...
" 20...	...	8	...	" 14...	8
" 21...	10	" 15...	...	6	Absent.
" 22...	...	8	...	" 16...	12
" 23...	15	" 17...	...	5	...
" 24...	...	8	...	" 18...	10
" 25...	10	" 19...	...	4	...
" 26...	...	14	Absent.	" 20...	6
" 27...	12	" 21...	...	4	Absent.
" 28...	...	11	...	" 22...	12
" 29...	8	" 23...	...	12	...
" 30...	...	4	...	" 24...	8
Dec. 1...	0	" 25...	...	8	...
" 2...	...	24	...	" 26...	6
" 3...	8	...	Absent.	" 27...	...	4	...
" 4...	...	10	...	" 28...	8
" 5...	6	" 29...	...	4	Absent.
" 6...	...	4	...	" 30...	2
" 7...	6	" 31...	...	0	...
" 8...	...	5	...	Feb. 1...	0
" 9...	5	" 2...	...	8	...
" 10...	...	4	Absent.	" 3...	6
" 11...	6	" 4...	...	4	Absent.
" 12...	...	4	...	" 5...	24
" 13...	3	" 6...	...	8	...
" 14...	...	8	...	" 7...	4
" 15...	4	" 8...	...	4	...
" 16...	...	6	...	" 9...	8
" 17...	5	...	Absent.	" 10...	...	14	...
" 18...	...	5	...	" 11...	4	...	Absent.
" 19...	4	" 12...	...	4	...
" 20...	...	4	...	" 13...	4
" 21...	8	" 14...	...	8	...
" 22...	...	5	...	" 15...	4
" 23...	10	" 16...	...	8	...
" 24...	...	2	Absent.	" 17...	12
" 25...	0	" 18...	...	4	Absent.
" 26...	...	0	...	" 19...	4
" 27...	12	" 20...	...	8	...
" 28...	...	15	...	" 21...	4
" 29...	15	" 22...	...	4	...
" 30...	...	15	...	" 23...	8
" 31...	12	...	Absent.	" 24...	...	4	Absent.
1904.				" 25...	5
Jan. 1...	...	8	...	" 26...	...	8	...
" 2...	20	" 27...	6
" 3...	...	5	...	" 28...	...	4	...
" 4...	6	" 29...	5
" 5...	...	5	...	Mar. 1...	...	12	...
" 6...	9	" 2...	6
" 7...	...	7	Absent.	" 3...	...	8	...
" 8...	2	" 4...	8	...	Absent.
" 9...	...	10	...	" 5...	...	4	...
" 10...	3	" 6...	5
" 11...	...	10	...	" 7...	...	6	...
" 12...	6				

EXPERIMENT 205. MONKEY (*Cercopithecus sp.*).

Feeding biting flies (Stomoxys) on a healthy monkey which had been fed 8 hours previously on a monkey infected with the trypanosomes of "Abyssinian fly disease."

Date.	Number of flies fed on : —		Tryp.	Date.	Number of flies fed on :—		Tryp.
	Infected Monkey.	Healthy Monkey.			Infected Monkey.	Healthy Monkey.	
1903.				1903.			
Sept. 27...	...	20	Absent.	Nov. 12...	16	14	Absent.
" 28...	16	15	...	" 13...	12	16	...
" 29...	13	0	...	" 14...	14	12	...
" 30...	23	18	...	" 15...	16	14	...
Oct. 1...	16	23	...	" 16...	16	11	...
" 2...	20	11	...	" 17...	16	14	...
" 3...	14	20	...	" 18...	14	12	...
" 4...	16	12	...	" 19...	26	24	Absent.
" 5...	17	20	Absent.	" 20...	20	10	...
" 6...	25	18	...	" 21...	20	8	...
" 7...	14	23	...	" 22...	14	18	...
" 8...	24	18	...	" 23...	12	10	...
" 9...	15	12	...	" 24...	14	8	...
" 10...	15	20	Absent.	" 25...	22	16	...
" 11...	20	14	...	" 26...	16	14	Absent.
" 12...	30	28	...	" 27...	16	20	...
" 13...	35	30	...	" 28...	12	15	...
" 14...	28	24	...	" 29...	14	10	...
" 15...	28	14	...	" 30...	18	10	...
" 16...	18	14	...	Dec. 1...	14	12	...
" 17...	20	18	Absent.	" 2...	10	20	...
" 18...	14	12	...	" 3...	12	8	Absent.
" 19...	10	11	...	" 4...	14	10	...
" 20...	16	17	...	" 5...	22	15	...
" 21...	14	12	...	" 6...	18	14	...
" 22...	18	10	Absent.	" 7...	22	16	...
" 23...	12	10	...	" 8...	18	12	...
" 24...	12	10	...	" 9...	14	10	...
" 25...	12	16	...	" 10...	12	6	Absent.
" 26...	9	12	...	" 11...	6	12	...
" 27...	12	10	...	" 12...	9	7	...
" 28...	14	12	...	" 13...	9	15	...
" 29...	10	8	Absent.	" 14...	16	14	...
" 30...	16	14	...	" 15...	12	11	...
" 31...	18	12	...	" 16...	12	14	...
Nov. 1...	14	10	...	" 17...	8	11	Absent.
" 2...	20	16	...	" 18...	6	7	...
" 3...	18	25	...	" 19...	8	12	...
" 4...	16	20	...	" 20...	5	10	...
" 5...	16	18	Absent.	" 21...	18	20	...
" 6...	18	14	...	" 22...	16	12	...
" 7...	10	0	...	" 23...	14	10	...
" 8...	18	14	...	" 24...	5	8	Absent.
" 9...	16	14	...	" 25...	0	0	...
" 10...	14	16	...	" 26...	8	5	...
" 11...	15	14	...	" 27...	15	10	...

Date.	Number of flies fed on :—		Tryp.	Date.	Number of flies fed on :—		Tryp.
	Infected Monkey.	Healthy Monkey.			Infected Monkey.	Healthy Monkey.	
1903.				1904.			
Dec. 28...	16	20	...	Feb. 17...	6	8	Absent.
" 29...	10	15	...	" 18...	3	6	...
" 30...	8	12	...	" 19...	2	3	...
" 31...	13	12	Absent.	" 20...	5	5	...
1904.				" 21...	4	5	...
Jan. 1...	8	6	...	" 22...	5	4	...
" 2...	10	8	...	" 23...	7	7	...
" 3...	11	12	...	" 24...	5	8	Absent.
" 4...	12	6	...	" 25...	4	6	...
" 5...	9	10	...	" 26...	6	8	...
" 6...	8	4	...	" 27...	4	6	...
" 7...	6	3	Absent.	" 28...	4	2	...
" 8...	18	3	...	" 29...	4	3	...
" 9...	4	4	...	Mar. 1...	4	6	...
" 10...	14	7	...	" 2...	4	4	...
" 11...	12	6	...	" 3...	6	7	...
" 12...	10	4	...	" 4...	5	5	Absent.
" 13...	6	5	...	" 5...	4	2	...
" 14...	6	4	Absent.	" 6...	4	8	...
" 15...	5	7	...	" 7...	3	4	...
" 16...	6	4	...	" 8...	6	6	...
" 17...	6	14	...	" 9...	3	8	...
" 18...	10	5	...	" 10...	6	5	...
" 19...	5	9	...	" 11...	5	7	Absent.
" 20...	6	6	...	" 12...	6	4	...
" 21...	4	4	Absent.	" 13...	8	4	...
" 22...	5	3	...	" 14...	5	8	...
" 23...	0	6	...	" 15...	4	6	...
" 24...	6	5	...	" 16...	5	8	...
" 25...	6	5	...	" 17...	14	10	...
" 26...	2	4	...	" 18...	14	11	Absent.
" 27...	4	3	...	" 19...	8	10	...
" 28...	3	2	Absent.	" 20...	5	12	...
" 29...	6	4	...	" 21...	10	10	...
" 30...	5	4	...	" 22...	14	12	...
" 31...	2	0	...	" 23...	10	7	...
Feb. 1...	4	9	...	" 24...	6	8	Absent.
" 2...	3	6	...	" 25...	4	5	...
" 3...	4	4	...	" 26...	8	10	...
" 4...	2	6	Absent.	" 27...	4	20	...
" 5...	8	10	...	" 28...	14	13	...
" 6...	6	12	...	" 29...	7	3	...
" 7...	6	4	...	" 30...	6	15	...
" 8...	8	4	...	" 31...	1	8	...
" 9...	11	6	...	Apr. 1...	14	4	...
" 10...	8	4	...	" 2...	10	8	...
" 11...	12	4	Absent.	" 3...	8	3	...
" 12...	6	5	...	" 4...	6	8	...
" 13...	6	5	...	" 5...	4	5	...
" 14...	6	8	...	" 6...	4	10	...
" 15...	16	12	...	" 7...	5	8	Absent.
" 16...	4	7	...	" 8...	3	5	...
				" 9...	3	12	...

Date.	Number of flies fed on :—		Tryp.	Date.	Number of flies fed on :—		Tryp.
	Infected Monkey.	Healthy Monkey.			Infected Monkey.	Healthy Monkey.	
1904.				1904.			
Apr. 10...	10	8	...	Apr. 21...	4	20	...
" 11...	5	3	...	" 22...	5	12	Absent.
" 12...	20	10	...	" 23...	6	10	...
" 13...	0	0	...	" 24...	3	8	...
" 14...	10	12	Absent.	" 25...	8	7	...
" 15...	10	8	...	" 26...	4	10	...
" 16...	12	14	...	" 27...	2	10	...
" 17...	11	10	...	" 28...	5	8	...
" 18...	14	11	...	" 29...	3	8	Absent.
" 19...	8	24	...	" 30...	6	12	Stopped.
" 20...	14	11	...				

EXPERIMENT 215. MONKEY (*Cercopithecus sp.*).

Feeding biting flies (*Stomoxys*) on a healthy monkey which had fed 8 hours previously on a monkey infected with the trypanosomes of the "mule disease."

Date.	Number of flies fed on :—		Tryp.	Date.	Number of flies fed on :—		Tryp.
	Infected Monkey.	Healthy Monkey.			Infected Monkey.	Healthy Monkey.	
Oct. 4...	8	18	Absent.	Oct. 24...	0	0	...
" 5...	13	10	...	" 25...	7	8	...
" 6...	12	9	...	" 26...	25	16	...
" 7...	14	12	...	" 27...	20	14	...
" 8...	12	15	...	" 28...	16	12	...
" 9...	5	9	...	" 29...	14	10	Absent.
" 10...	20	35	...	" 30...	14	12	...
" 11...	28	24	Absent.	" 31...	12	10	...
" 12...	28	10	...	Nov. 1...	10	11	...
" 13...	24	35	...	" 2...	9	12	...
" 14...	26	28	...	" 3...	16	14	...
" 15...	27	20	...	" 4...	14	12	...
" 16...	28	12	...	" 5...	18	10	Absent.
" 17...	0	0	Absent.	" 6...	16	12	...
" 18...	0	0	...	" 7...	15	0	...
" 19...	0	0	Absent.	" 8...	11	14	...
" 20...	0	0	...	" 9...	14	10	...
" 21...	0	0	...	" 10...	12	11	Absent.
" 22...	0	0	Absent.	" 11...	26	10	Stopped.
" 23...	0	0	...				

As a result of the above experiments it may be considered proved that the *Glossina palpalis* can convey the above trypanosomes from the sick to healthy animals and so propagate the disease. Apart from the great practical importance attached to this, it is also of considerable interest to note that the *Glossina palpalis* can convey not only the *Trypanosoma gambiense*, but other varieties. This being so, it is reasonable to suppose also, that other varieties of *Glossina* will convey the *Trypanosoma gambiense*. This being so, it will be evident from Mr. Austen's map that a very extensive tract of country will be involved. At Igaga's and Kibui, halting places of the Jinja cattle, a variety of tsetse fly (*Glossina pallidipes*) was found.

It may be, further, considered proved that (*Stomoxys*) cannot convey these trypanosomes from the sick to the healthy animals. This is a matter of great practical importance also, because these flies abound in Uganda.

Some observations were made on the length of time which the various trypanosomes remain active in the stomach of the fly. The contents of the stomach, food reservoirs and salivary glands have been studied both fresh and by staining, but no definite life cycle has been observed in the parasites. In the ventral food reservoir active trypanosomes have been seen up to 12 hours after feeding. This is interesting in view of the fact stated by Schaudinn, that mosquitoes discharge the contents of the sac into the wound, in fact the irritation is produced by these contents.*

Experiments were made to see whether the *Glossina palpalis* can convey any of these varieties of trypanosomes after longer intervals (5 days and over). These remained entirely negative. So it would appear that if the trypanosoma undergoes any transformation in the body of the fly as Schaudinn's work suggests, it must be a short one.

A point of considerable interest in connection with the flies is the tendency which they have to "abort" in captivity. Mr. Austen drew attention to the great variation in size of the pupæ in some specimens sent to him and put forward the above explanation. To test this a number of pupæ have been placed in suitable places and their development noted. It was found that the small undersized specimens underwent no further alteration, whilst the larger and normal looking pupæ hatched out as usual. This would thus suggest that the small pupæ had been prematurely laid and were not viable.

APPENDIX.

In the further report, the histories of a number of cases of sleeping sickness were given; an additional series have been

* This portion of the investigation, which is very technical, will be elaborated by Professor Minchin, who has gone to Uganda for this purpose.

recorded. In the following cases the special point which has been investigated is the relationship of bacterial invasion to the disease, the frequency and stage of the disease at which it takes place; a more detailed study of the blood is given. Also the results of the examination of the lymphatic glands are given *in extenso*.

The following are the histories:—

CASE $\frac{69}{60}$ SABAKAKI (MALE), AGE 8 YEARS.

February 28, 1904. Patient admitted into hospital to-day. Superficial lymphatic glands enlarged. He presents a dull facial expression, with tremors of the tongue and hands. He complains of itching, and there are scratch marks. The pulse is 84, fair.

March 6th. No noteworthy alteration in patient's condition. He is in the late second stage of the disease.

March 15. A gland was excised from the left posterior triangle of neck. The juice contained active trypanosomes, but no diploeocci.

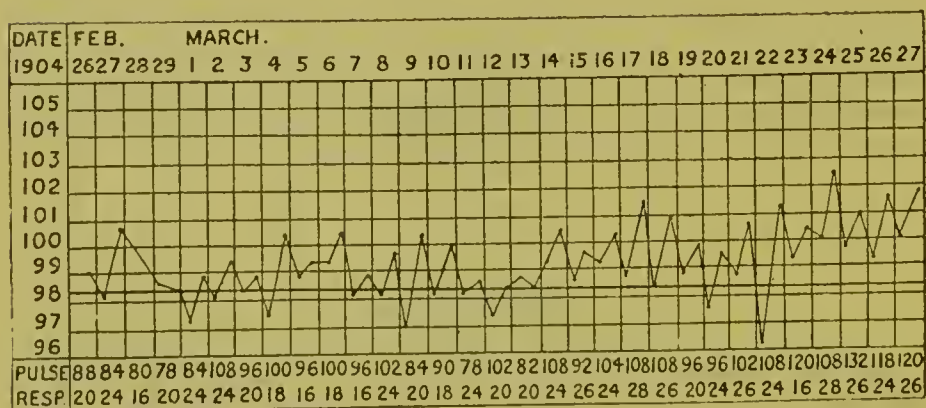
May 15. The general condition of the patient is worse. Pulse 104, tension low. Heart sounds are normal.

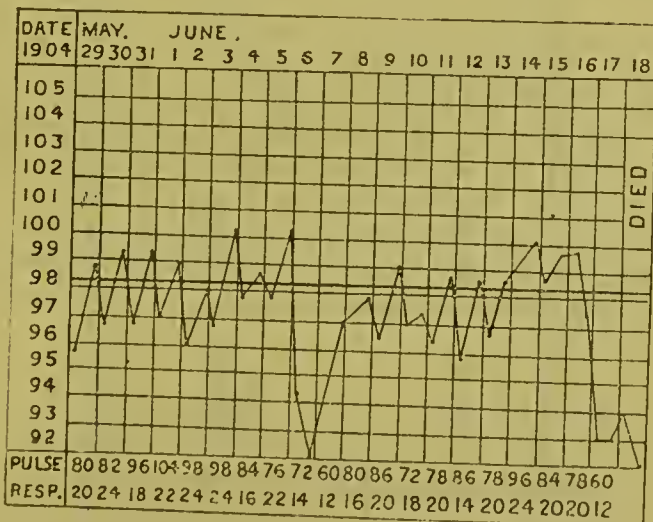
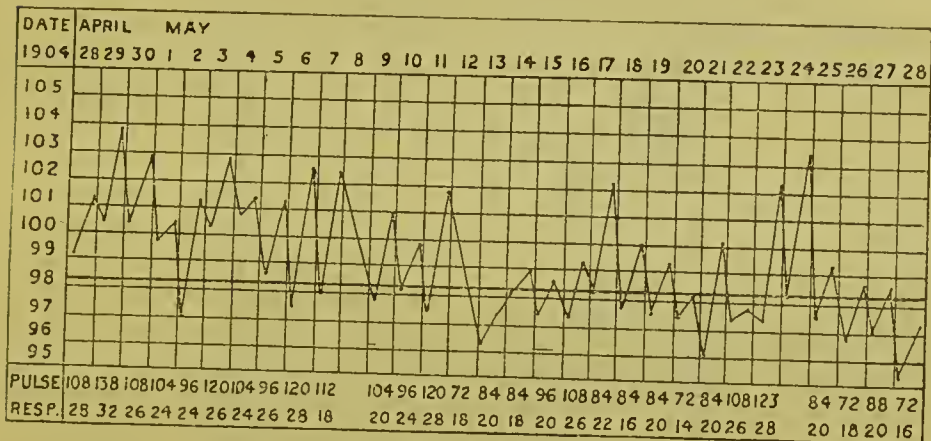
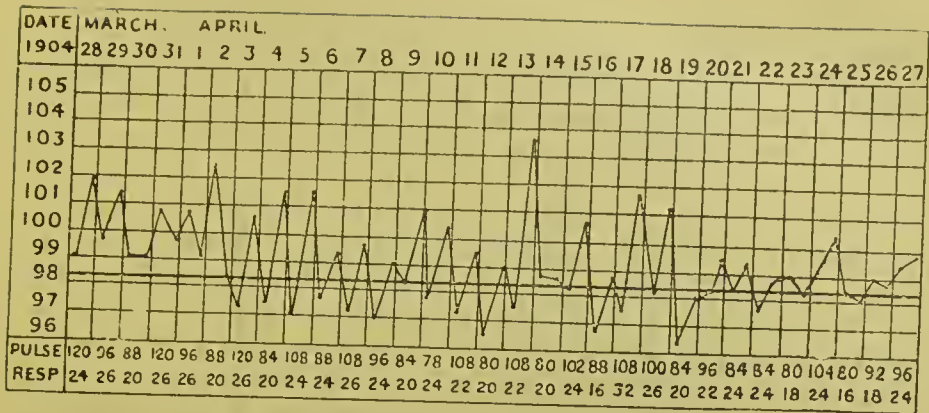
May 27. The patient is passing into the third stage of the disease.

June 6. The patient is now very emaciated and completely bedridden. Jiggers in both feet. The glands in the left posterior triangle of neck were punctured. A tube of broth inoculated with the juice remained sterile. The juice contains many active trypanosomes and also on staining some disintegrating forms. The cerebro-spinal fluid contained active trypanosomes and 94 cells, all mono-nuclear, per cmm.

June 14. The patient is moribund.

The following chart represents the course of the disease:—





The following table shows the result of the enumeration of the blood corpuscles, the percentage of hæmoglobin and the presence or absence of diplococci and trypanosomes in the glands, blood and cerebro-spinal fluid :—

Date.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.
			P.N.	S.M.	L.M.	E.		Strept.	Tryp.	Fil.	Mal.	Tryp.	
1904.													
March 15	32	37	31	-	+	+	-	-	+
June 6	...	3,700,000	57	34	9	...	68	-	+	-	-	-	+
" 18	-	+	-	-	-	..

June 18. Died. Post-mortem.

The body is markedly emaciated. There is general enlargement of the superficial lymphatic glands. There are jiggers in both feet. The pupils are equal and normal. There is no increase of fluid in pleural, pericardial or peritoneal cavities.

On removing the calvarium and reflecting the dura mater some flattening of the convolutions is noticed. There is an increase of sub-arachnoid fluid, giving a dull appearance to the membrane. Spinal cord shows nothing noteworthy to the naked eye. Portions of brain and spinal cord with nerve roots ganglion and nerves were removed for minute investigation. A culture in broth of the cerebro-spinal fluid remained sterile.

Heart.—Shows no noteworthy change. A culture from the blood of this organ shows the presence of *B. coli communis*.

Lungs.—Both show minute areas of embolism scattered throughout, being both subpleural and in the deeper tissue.

Liver.—Shows some congestion.

Spleen.—Distinctly enlarged and pigmented.

Kidneys.—Show no noteworthy change.

Glands.—There is very marked enlargement of both femoral and inguinal groups; these are continuous with a chain which runs along the large vessels of the abdomen towards the thorax; the thoracic group are continuous above with the cervical chain, which extends up to the suboccipital region. No points of suppuration are present in the glands. A culture in broth of the gland juice remained sterile. Stained preparations of the juice showed altered trypanosomes.

Stomach.—Mucous membrane was studded with dark points surrounded by a zone of light red, these petechiæ were more marked towards the pyloric orifice.

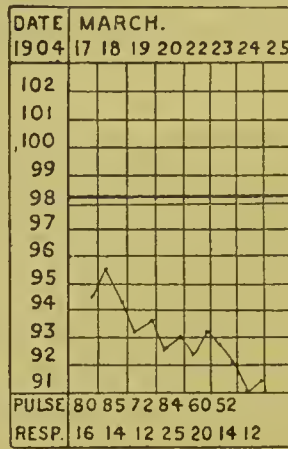
Remarks.—This case is of interest as showing that here there was no invasion by the diplococcus. The *B. coli communis* in this case invaded the tissues probably very shortly before death. This case was therefore one of trypanosoma infection from the beginning to the end. The condition of the lungs was interesting, embolism being a common post-mortem sign in trypanosomiasis of animals.

The condition of the mucous membrane of the stomach was remarkable in this case, compare cases Geerude and Zakayo.

CASE $\frac{69}{99}$ ZERIDAN (MALE). AGE 16 YEARS.

March 17, 1904. Admitted to hospital. Facies dull and expressionless. Gait is very uncertain. Tremors of hands. Pulse 80, feeble. No oedematous swellings. Lymphatic glands generally are enlarged to a considerable extent. Patient is in the third stage of the disease. Lymph glands were excised from the left posterior triangle of the neck. The juice was examined microscopically and cultures were made in broth and agar from it.

March 20. Patient is now in a moribund condition.
The following chart represents the course of the fever:—



The following table shows the presence or absence of trypanosomes and streptococci in the lymphatic glands and cerebro-spinal fluid, also the total and differential leucocytes count:—

Date.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.	
			P.N.	S.M.	L.M.	E.		Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.
1903.														
March 17	15,600	45	39	14	2	...	-	+	-	-	-	+
" 24	+	+	-	+	+	...

March 24. Died. Post-mortem.

The body is covered with a number of blebs containing purulent fluid. No bedsores. The lymphatic glands are generally enlarged.

On opening the body no increase of pleural, pericardial, or peritoneal fluid is found.

Brain.—The sub-arachnoid fluid is increased, giving a dull ground glass appearance. The superficial vessels are injected. The appearance is typical of a sleeping sickness brain. The cerebro-spinal fluid was inoculated into broth and agar tubes, and a pure culture of diplococci was obtained.

Heart.—Normal; a culture in broth and agar from the blood in this organ gave a pure culture of diplococci.

Lungs.—Both normal.

Spleen.—Slightly enlarged, no pigmentation.

Kidneys.—Both rather pale.

Glands.—The juice of the lymph glands examined under the microscope showed the presence of diplococci; no living trypanosomes were seen, but structures which were, probably, broken down trypanosomes.

Remarks.—This case is of interest as showing that the invasion of tissues of this patient by the diplococcus must have occurred just before death, being merely, therefore, a terminal invasion and standing in no causal relation to the disease in this case. The lymph juice examined on March 17 showed the presence of active trypanosomes, but not of cocci, although cultures were made from the glands: the examination of the glands post-mortem, eight days later, showed the presence of streptococci. The heart's blood and cerebro-spinal fluid also contained these.

CASE $\frac{69}{RR}$ ABIMERIKA (MALE). AGE 22 YEARS.

February 27, 1904. Patient was admitted to hospital. He has general enlargement of the lymphatic glands. Facial expression is dull. There are tremors both of tongue and hands.

March 6. The facial expression is duller than before.

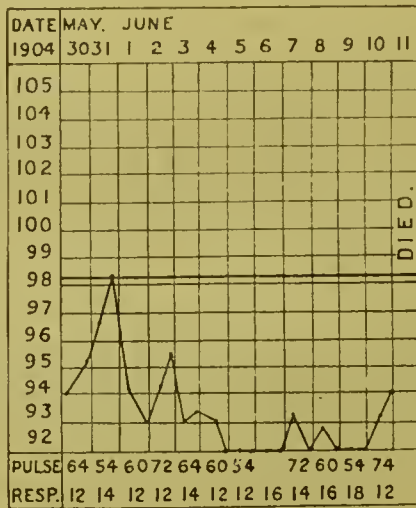
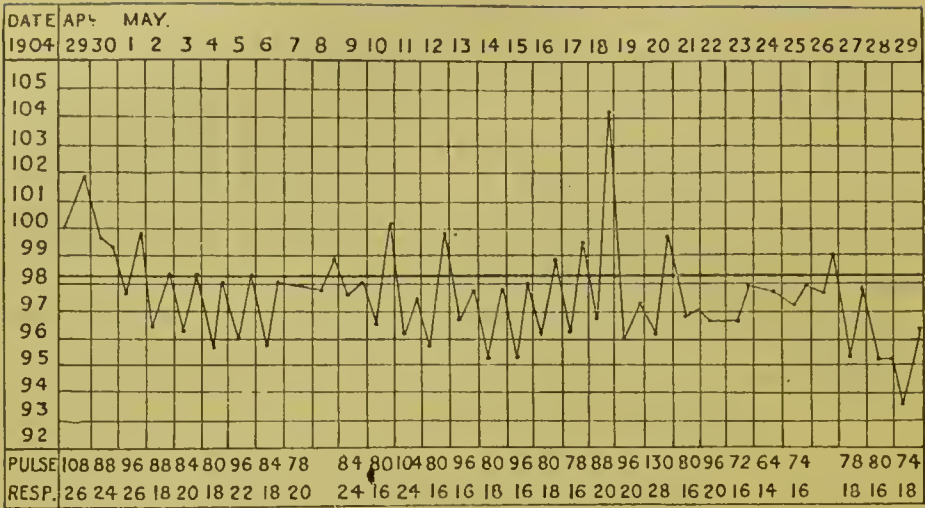
March 18. Three superficial glands were excised from the right posterior triangle of neck. Two enlarged glands were also removed from the left femoral region.

Cultures made from the juice in broth and agar remained quite sterile.

April 21. A gland in the left post triangle was punctured—the juice examined microscopically showed active trypanosomes, but no streptococci.

May 15. The facial expression is now very dull. The gait is very uncertain. Heart sounds are weak. There are general tremors of the body. The appetite is good. The pulse is 86; tension low. Patient is passing into the third stage.

May 27. The patient is distinctly in the third stage. He



The following table shows the result of enumeration of the blood cells, the presence or absence of diplococci and trypanosomes from the lymphatic glands, blood and cerebro-spinal fluid:—

Date.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.	
			P.N.	S.M.	L.M.	E.		Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.
1904.														
Feb. 27	+
March 19	...	8,600	50	27	13	10	...	-	+	-	-	-
April 11	5,200,000	15,600	22	58	6	14	-	-	-
" 21	5,300,000	13,900	29	48	15	13	84	-	+	-	-	-
May 10	5,000,000	13,700	24	25	43	8	90	-	-	-
" 31	5,000,000	9,370	35	21	28	16	80	-	-	-
June 4	5,300,000	10,000	32	27	38	3	90	-	+	-	-	+
" 11	+	+	-	-	-

June 11. Died. Post-mortem.

The body is somewhat emaciated. There is general enlargement of the superficial lymphatic glands. Sores, due to jiggers, are present in both feet. The pupils are equal and normal. On dividing the abdominal wall above the pubis a large mass of yellow jelly-like material, which infiltrates between the layers of muscles, is seen. This material under the microscope did not show active trypanosomes. There is no increase of fluid in the pleural, pericardial, or peritoneal cavities.

Brain.—On removing the calvarium and reflecting the dura mater some increase of sub-arachnoid fluid is noticed, giving a dull appearance to the membranes, especially towards the base; spinal cord with roots and ganglion removed, along with portions of the brain and glands for minute study.

Heart.—Rather pale, otherwise healthy. Cultures from the blood of this organ made in broth and agar. Both showed a pure growth of a coccobacillus, probably *B. coli*.

Lungs.—Nothing noteworthy.

Liver.—Congested, otherwise nothing noteworthy.

Spleen.—Shows old perisplenitis; it is enlarged, and on section is seen to be pigmented.

Kidneys.—Nothing noteworthy.

Glands.—All the groups of glands are markedly enlarged, those in the femoral region especially so. In the left femoral region the glands show small points of suppuration—no points of suppuration in the cervical or other glands. The abdominal glands are markedly enlarged and congested on section.

The juice from the cervical glands was inoculated into tubes of broth. The microscopic examination showed no active trypanosomes or diplococci, but some modified trypanosomes were seen in the stained preparations. No growth could be obtained from the juice of the cervical glands in broth.

Remarks.—This case is of interest as showing that the diplococcic invasion was not general: the heart's blood post-mortem showed an invasion by *B. coli communis* and no diplococci. The diplococcic invasion was very localised, being limited to the left femoral group of glands which showed points of suppuration. The other groups showed no cocci.

CASE 69, WASIWA (MALE). AGE 18 YEARS.

V.V.

January 1, 1904. He presents the usual features of the second stage of sleeping sickness. He is well nourished. There is general enlargement of superficial lymphatic glands. There is marked tremor of tongue. The facial expression is dulled.

February 28. The general condition of the patient shows no noteworthy alteration.

March 26. Lymphatic glands were removed to-day from the left posterior triangle of neck and from right femoral

region. Both the glands contained active trypanosomes. There is some œdematous swelling of the feet.

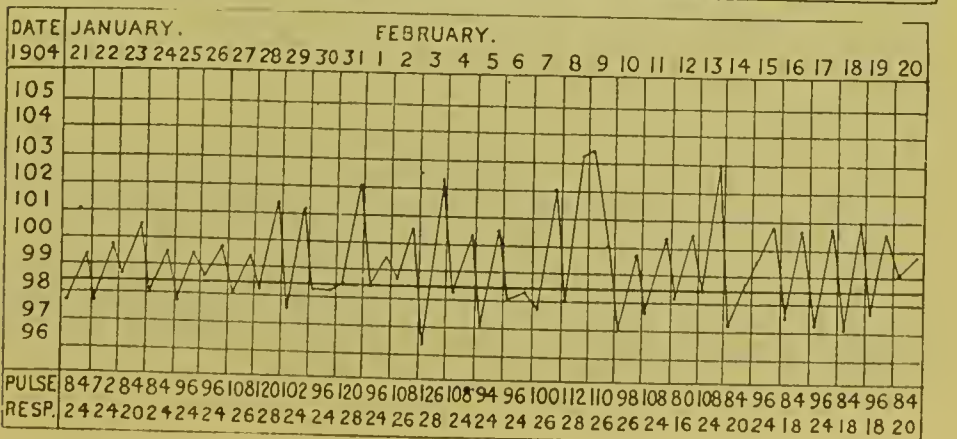
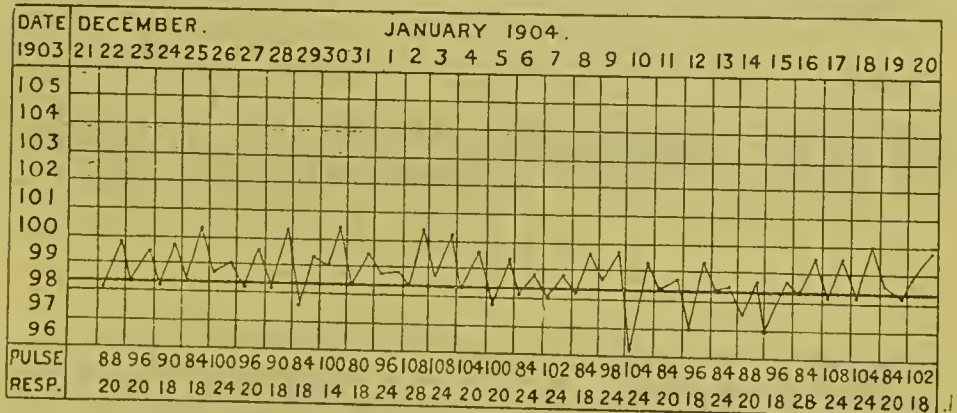
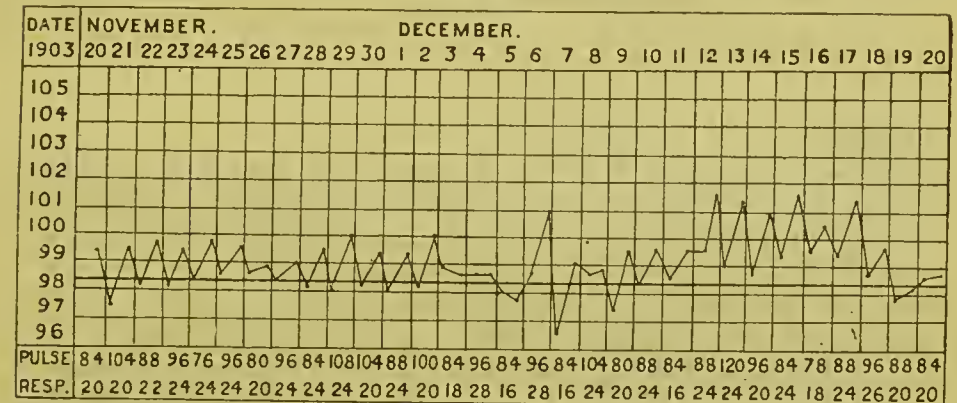
May 15. The expression of face is now very dull. The tremor of his tongue is marked. The appetite is good. The heart sounds are normal. Pulse 84, tension low. Itching of skin is present.

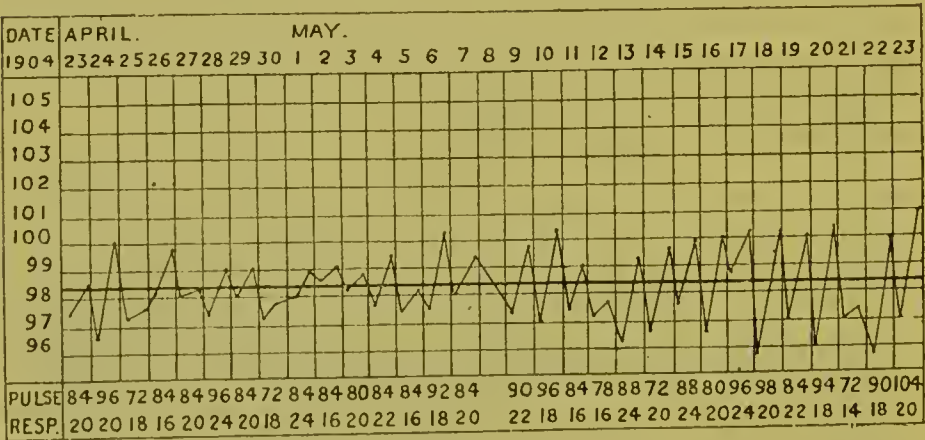
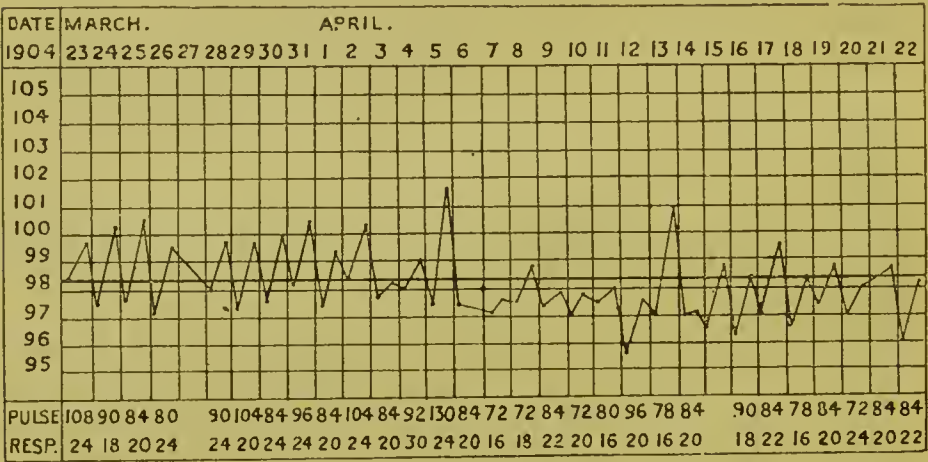
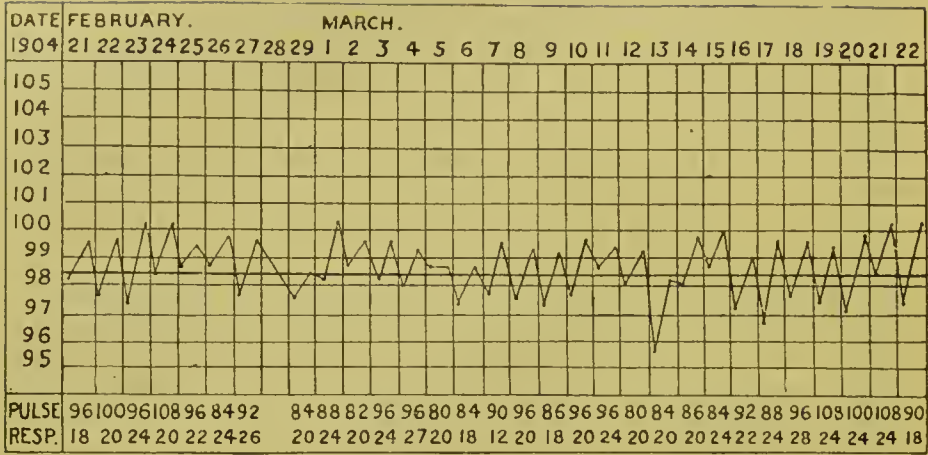
May 27. The general condition shows no noteworthy change.

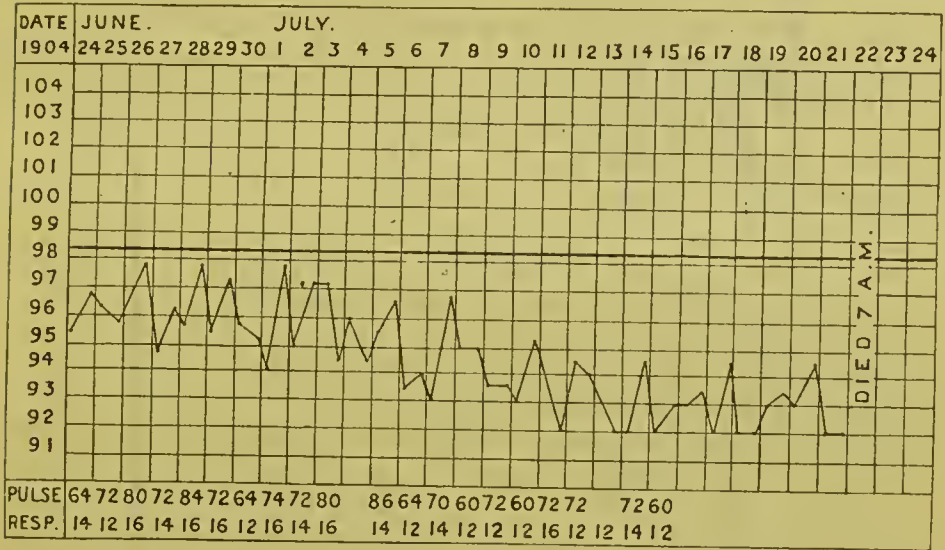
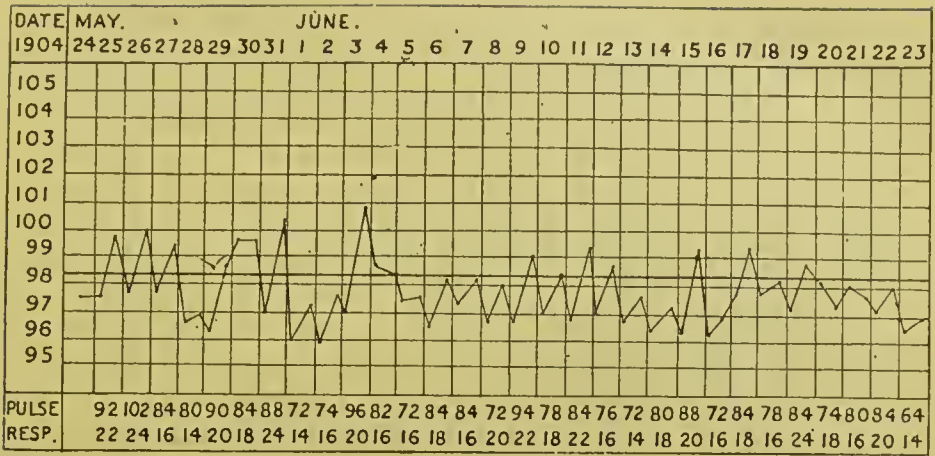
June 26. The patient is getting gradually weaker. He is now in third stage of this disease.

June 30. The patient is now completely bedridden. A lymphatic gland was excised from the right posterior triangle of the neck. The juice was found to contain active trypanosomes. Cultures were made in agar and in broth; both remained sterile.

The chart shows the course of the disease :—







The following table shows the result of enumeration of the blood corpuscles, the percentage of hæmoglobin, the presence or absence of streptococci and trypanosomes in the lymphatic glands, blood and cerebro-spinal fluid :—

Date.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.	
			P.N.	S.M.	L.M.	E.		Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.
1904.														
March 25	13,400	49	29	8	14	...	-	+	-	-	-	-	+
April 19 ...	5,300,000	11,200	33	49	9	10
June 8 ...	5,300,000	10,300	37	40	15	8	94
" 30 ...	5,500,000	11,200	48	44	4	4	92	-	+	+	-	-
July 16 ...	5,700,000	7,800	52	31	16	1	95	+	...	-
" 22	-	+	-	...

July 22. Patient died. Post-mortem.

The body is very well nourished. General enlargement of superficial lymphatic glands. Jiggers in both feet. The wound on right side of neck is not completely healed.

No increase of fluid in the pericardial, pleural, or peritoneal cavities.

Brain.—On removing the calvarium and reflecting the dura mater, it is seen that the sub-arachnoid fluid is increased, giving a ground glass appearance to the membranes, the superficial vessels are injected. The ventricles are dilated and there is an increase of fluid in them. The spinal cord presents no noteworthy naked-eye change. Portions of the brain and spinal cord were preserved for minute examination. A culture was made from the cerebro-spinal fluid in broth. This remained sterile.

Heart.—Under the endocardium of the left ventricle several petechiæ are seen to be present. The muscle substance is pale. A culture in broth from the heart's blood remained sterile.

Lungs.—Right is congested, left is healthy.

Liver.—Shows a condition of advanced chronic venous congestion, with fatty changes at the periphery of the lobules.

Spleen.—There is some periplenitis; organ is somewhat enlarged. It is pigmented on section.

Kidneys.—Both show early chronic venous congestion.

Glands.—All the groups are enlarged. The femoral shows points of suppuration (from the sores in feet). No points of suppuration in the cervical glands. A culture in broth from a gland in the left posterior triangle remained sterile. Smears from the cervical glands showed no diplococci. They are present in the femoral glands.

Remarks.—This case again is one of pure trypanosome infection. Streptococci were only present in the enlarged femoral glands, having obtained entrance by the jigger sores.

CASE 69 KIRONGO (MALE). AGE 40 YEARS.
W.W.

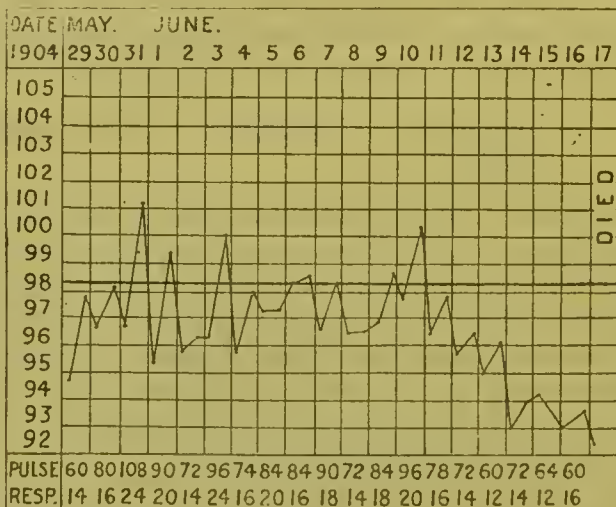
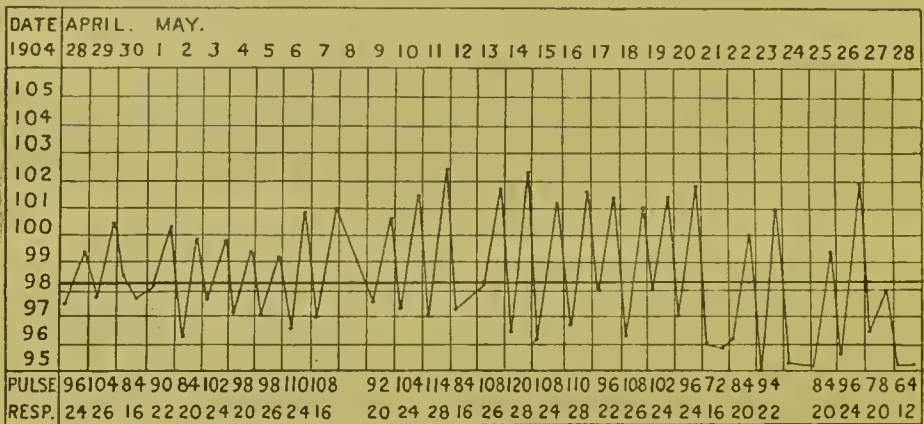
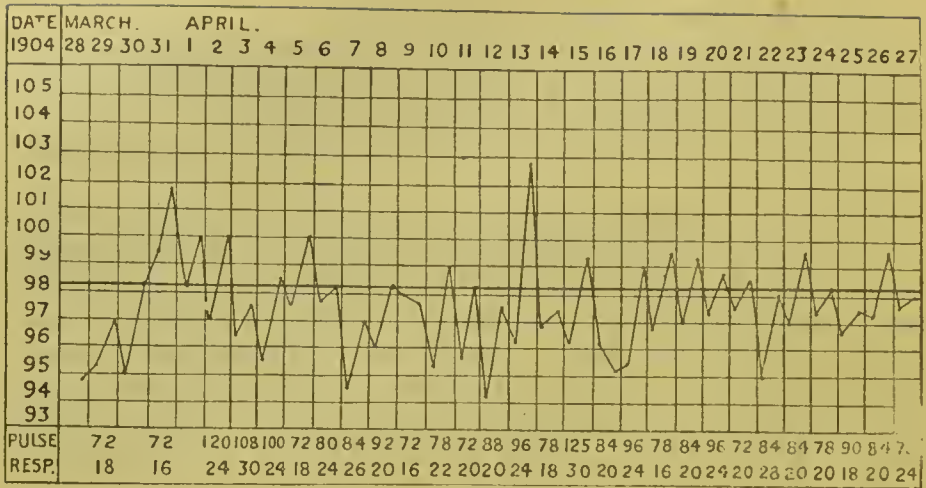
March 23, 1904. The patient looks an old man. He has very distinct general enlargement of lymphatic glands. There are tremors of both tongue and lips. The heart sounds are normal. Pulse 120, weak. Appetite is good. The glands in the right femoral region and also in the left posterior triangle of neck were punctured and in both active trypanosomes were found. No diplococci could be detected microscopically. Cultures in broth from the gland juice remain sterile.

May 15. The wounds in the neck and femoral region, which had suppurated, have now completely healed up. There are jiggers in both feet.

May 27. The patient is now passing into the third stage.

June 12. The condition of patient is more pronounced. He is definitely in the third stage.

The following chart shows the course of the disease:—
(7390)



The following table shows the result of enumeration of the blood corpuscles, the percentage of hæmoglobin, the presence or absence of diplococci and trypanosomes in the lymph glands, blood and cerebro-spinal fluid:—

Date.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.	
			P.N.	S.M.	L.M.	E.		Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.
1904.														
March 28	51	35	10	4	+	-	-	..	+	
April 25	...	4,900,000	25	50	17	8	82	+	
" 12	...	5,400,000	54	37	4	5	
June 14	...	4,400,000	30	41	15	14	84	+	...	
" 17	+	...	

June 16. Patient died. Post-mortem.

There is a general enlargement of superficial lymphatic glands. Sores in both feet due to jiggers. There is not much emaciation. The pupils are equal and normal. No increase of fluid in the pleural, pericardial, or peritoneal cavities.

Brain.—On removing the calvarium and reflecting the dura mater the sulci are seen to be filled up with a turbid exudation. The superficial vessels are injected. Towards the base of the brain the exudation is more marked. The lateral ventricles are dilated and there is an increase of cerebro-spinal fluid. The spinal cord shows nothing noteworthy. Portions of the nervous system removed for further examination.

The exudation examined microscopically shows the presence of diplococci; a culture made in broth and agar showed a fine growth, probably pneumococcus.

Heart.—Old endocarditis of mitral valve present, otherwise nothing noteworthy. A culture in broth from the blood of this organ was made and showed the presence of the *bacillus coli communis*.

Lungs.—Both apparently healthy.

Liver.—Adherent in places to diaphragm. On section it shows a condition of chronic venous congestion with commencing cirrhosis.

Spleen.—Somewhat enlarged and very markedly adherent to surrounding parts. The capsule is thickened.

Kidneys.—Both show a condition of chronic venous congestion.

Glands.—Deep cervical and suboccipital are markedly enlarged. They were removed along with cervical nerves for minute investigation.

Remarks.—This case is of interest as showing that although the patient was in a late stage of the disease at the time of examination no diplococci were present in the glands, but many active trypanosomes were found. On post-mortem examination a diplococcus was observed in the exudation in the brain. This must have occurred at a late stage of the disease, when the patient was practically moribund.

CASE 69 XX. ZUMAGEZA (MALE). AGE 18 YEARS.

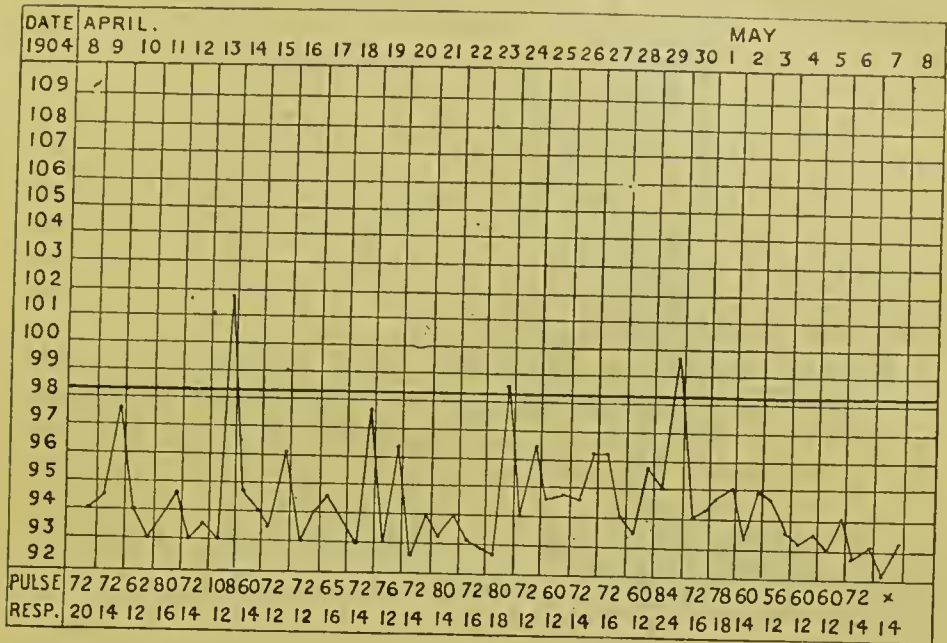
April 9, 1904. Admitted into hospital, sent by Dr. J. H. Cook. Patient presents a markedly dull facies and tremors of tongue; lymphatic glands are generally enlarged. He has a chronic synovitis of right wrist. A gland in the left posterior triangle of neck was punctured and the juice examined microscopically showed active trypanosomes; no streptococci could be seen in stained films of the juice. 10 c.c. cerebro-spinal fluid placed in broth; it remained sterile.

April 20. Punctured cervical glands again.

April 30. Patient is getting distinctly worse and is in the third stage of the disease.

May 8. Died to-day.

The following chart represents the course of the disease:—



The following table shows the presence or absence of trypanosomata and streptococci in the blood, lymphatic glands, and cerebro-spinal fluid, also the results of the red and white blood corpuscles:—

Date.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in blood.			Parasites in glands.		Parasites in C.S.F.		
			P.N.	S.M.	L.M.	E.		Fil.	Mal.	Tryp.	Strept.	Tryp.	Strept.	Tryp.	
1904.															
April 9	50	40	9	1	...	-	-	-	-	+	-	+	...
" 20	...	4,200,000	57	31	12	0	65	-	-	-	-	+
May 8	+	+

May 8. Post-mortem.

The body is not emaciated, there is general enlargement of the superficial lymphatic glands. Right wrist is swollen and there is a fistulous opening over the ulna leading down to bone. On exposing the joint, the articular surface of the ulna and scapal bones were seen to be eroded and ulcerated. The synovial membrane was in a jelly-like condition. On opening the body there was no increase of fluid in the pleural, pericardial or peritoneal cavities.

Brain.—Some increase of sub-arachnoid fluid. The pia mater looks like ground glass and the sulci are filled with fluid. There is some injection of the superficial vessels. Spinal cord shows nothing noteworthy to the naked eye. Portions with roots and ganglion attached as well as parts of the brain and glands were removed for minute investigation.

Heart and Lungs.—Nothing noteworthy, naked eye.

Liver.—Shows congestion.

Spleen.—Enlarged, pigmented and firm on section.

Glands.—Cervical and suboccipital were markedly enlarged and congested. They formed a continuous chain from the cranium to the thorax following the course of the main vessels. Small points of suppuration are seen on section. Examined microscopically the lymphatic glands are seen to contain diplococci and broken down trypanosomes.

Remarks.—This is an ordinary case of sleeping sickness. It is of interest to note that when juice from the enlarged glands of the neck was examined less than a month before death, when the disease was in its last stage, the only parasites seen to be present were trypanosomes; no streptococci were observed at that date. However, 18 days later minute points of suppuration were found in the glands, and diplococci invaded the tissues probably just before death and could have played, therefore, no part in the causation of the symptoms which are met with in an advanced case of sleeping sickness.

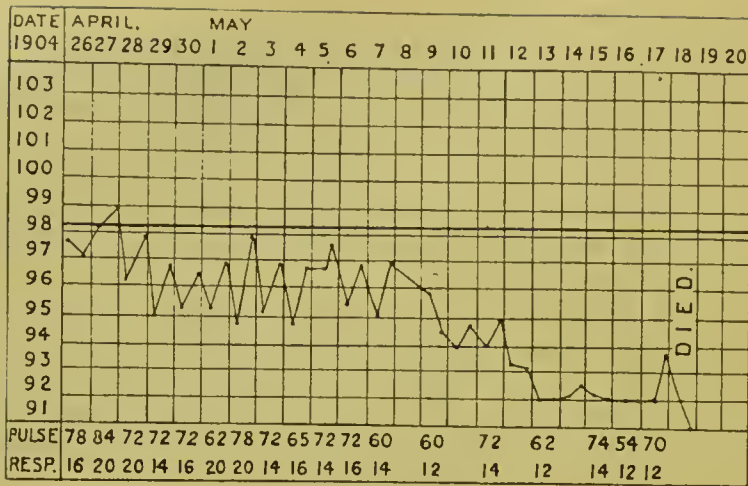
CASE $\frac{69}{22}$ USMANI (MALE). AGE 20 YEARS.

April 25, 1904. Admitted to hospital. Glands in the right anterior triangle of neck were punctured.

May 9. Patient is practically bed-ridden, being unable to walk. The superficial glands are generally enlarged. The facies is dull and heavy. He sleeps frequently. The glands were punctured in the right anterior triangle of neck. 10 c.c. cerebro-spinal fluid placed in broth; it remained sterile.

May 15. The patient is now in a moribund condition. He sleeps constantly.

The following chart represents the course of the disease:—



The following table shows the result of the enumeration of the blood cells and the presence or absence of streptococci and trypanosoma in the lymphatic glands, blood, and cerebro-spinal fluid :—

Date.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.	
			P.N.	S.M.	L.M.	E.		Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.
1904.														
April 25
May 9
" 19

May 19. Died. Post-mortem.

The body is somewhat emaciated. The superficial glands are generally enlarged.

On opening the body there is no increase of fluid in the pleural, pericardial, or peritoneal cavities.

Brain.—On removing the calvarium and reflecting the dura mater some increase of sub-arachnoid fluid was noticed, giving a dull appearance to the membranes. No streptococci were detected in film smears. Portions of brain and spinal cord were preserved for minute investigation.

Heart.—Nothing noteworthy.

Lungs.—Healthy.

Liver.—Some old adhesions over the surface and about the gall-bladder, on section nothing noteworthy.

Spleen.—Distinctly enlarged; the juice examined microscopically showed no streptococci.

Kidneys.—Both normal.

Lymphatic glands.—Mesenteric are distinctly enlarged. The deep cervical are markedly enlarged: on section to the naked eye show no points of suppuration. The expressed juice examined under the microscope in the fresh and stained specimens showed no active trypanosomes in the former, in the latter altered trypanosomes, but no streptococci could be seen.

Remarks.—The examination of this patient's glands about 24 hours before death showed the presence of active trypanosomata, but no streptococci. Further, in this case an investigation of the juice of the various organs post-mortem showed that the streptococci were not present. No points of suppuration were seen on section of the glands. This was a case of pure trypanosoma infection from first to last with no terminal invasion. The red blood corpuscles rose in this case to 5,600,000 per mm³., the percentage of hæmoglobin to 110.

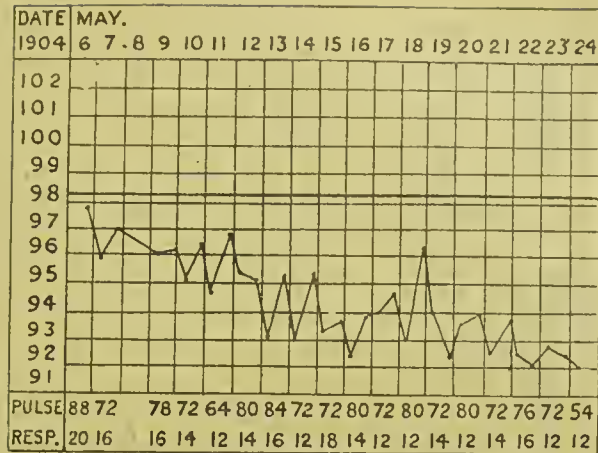
69
CASE $\frac{\text{G.T.}}{\text{G.T.}}$ MASAKE (MALE). AGE 16 YEARS.

May 6, 1904. Patient admitted to hospital. The lymph glands in the right posterior triangle of neck were punctured and juice drawn off. 10 c.c. cerebro-spinal fluid placed in broth; it remained sterile.

May 7. Patient lived at Buganga near Entebbe. States he has been ill one month. On examination he presented a dull facial expression with tremors of hands. The lymphatic glands were generally enlarged. Pulse 88. Heart sounds normal. Spleen slightly enlarged. Liver not enlarged.

May 15. The patient is distinctly in the third stage of the disease. His gait is ataxic. Expression of face is very dull. General tremors of body are present.

The following chart represents the course of the disease:—



The following table shows the result of the blood corpuscle enumeration, the presence or absence of streptococci or trypanosoma in the glands, blood and cerebro-spinal fluid :—

Date.		R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in the blood.			Parasites in C.S.F.	
				P.N.	S.M.	L.M.	E.		Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.
1904.															
May	6	49	17	25	9	75	-	+	-	-	+	-	+
"	7	-	+	-
"	9	-	+	-
"	11	-
"	13	-
"	24	-	+

May 24. Died. Post-mortem.

The body is not much emaciated. The superficial glands, especially in the axilla, are distinctly enlarged. In the groin and axilla they are extremely congested, and some even show small areas of hæmorrhage, though no points of suppuration can be seen in any of the glands.

On opening the body no increase of fluid in pleural, pericardial or peritoneal cavities is seen.

Brain.—On removing the calvarium and reflecting the dura mater some increase of sub-arachnoid fluid is seen. The pia mater has a ground-glass appearance. Some injection of superficial vessels.

Heart.—Nothing noteworthy.

Lungs.—Both show hypostatic congestion at posterior surface.

Liver.—Shows early cirrhosis.

Spleen.—Slightly enlarged, firm on section, not pigmented.

Kidneys.—Both healthy.

Glands.—Culture was made from the right cervical glands in broth; this remained sterile, no diplococci could be seen under the microscope. No active trypanosomes were seen, but broken down forms were noted in the stained specimens.

Remarks.—This was a fairly active case. The examination of the lymph juice *intra vitam* on May 6 showed the presence of active trypanosome, but no streptococci.

On post-mortem examination of the glands no diplococci could be cultivated from the cervical glands, altered trypanosomes were seen in the stained specimens.

Sections of the various organs were made and stained for micro-organism; no diplococci or other bacteria were observed. This was a case of pure trypanosoma infection.

CASE 69 F.V. HAMISI (MALE). AGE 12 YEARS.

May 5, 1904. The patient was admitted into hospital to-day.

May 7. He states that he has been sick for about one month. He lives in a shamba near the Lake close to Entebbe. His food is bananas and potatoes. He had headache at the beginning of the illness. He presents now a heavy dull facial expression. No tremor of hands—slight tremor of tongue. The knee jerks are normal, no ankle clonus. The superficial lymphatic glands are generally enlarged. His pulse is 108.

Heart.—Sounds normal.

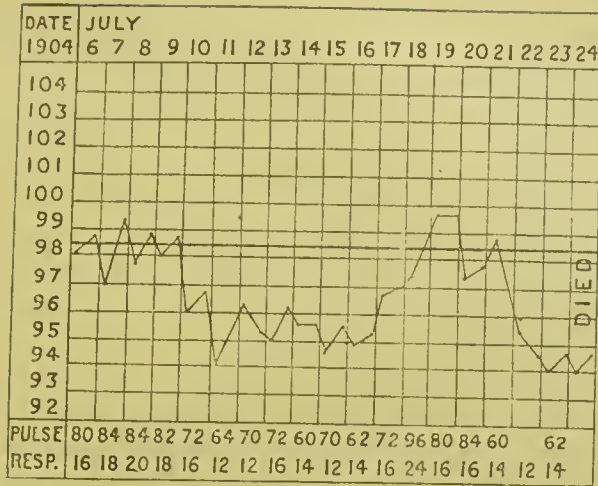
Lungs.—Normal.

Liver.—Is not enlarged.

Spleen.—Extends to the costal margin.

May 15. The general condition shows no alteration. He is somewhat excited.

May 27. The patient is distinctly in the second stage of the disease.



The following table shows the results of the enumeration of the blood corpuscles, the percentage of hæmoglobin, the presence or absence of trypanosomes and streptococci in the glands, blood and cerebro-spinal fluid:—

Date.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in the blood.			Parasites in C.S.F.		
			P.N.	S.M.	L.M.	E.		Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.	
1904.															
May 5	...	3,800,000	52	27	16	5	64	-	+	-	+	+	-	+	...
" 16	...	4,000,000	35	32	28	5	60	+	+	+
" 19	31	37	22	10	+	+	+
June 16	...	5,200,000	50	34	11	5	78	-	+	+
" 22	49	36	12	3	+	+
" 23	+
July 12	...	5,000,000	54	32	13	1	78	-	+	+	+	+
" 20	...	5,400,000	65	24	11	...	84	+	+	+
" 24	+	+

July 24. Patient died. Post-mortem.

The body is markedly emaciated. Jiggers present in both feet and hands. The pupils are equal and normal.

There is no increase of fluid in the pericardial, pleural or peritoneal cavities.

Brain.—On removing the calvarium and reflecting the dura mater, the convolutions are seen to present the usual appearance of a sleeping sickness brain. The sub-arachnoid fluid is considerably increased, giving the usual ground glass-like appearance to the membrane. This is more marked towards the base. The superficial vessels are injected. The lateral ventricles are dilated. The substance of the brain shows points of congestion throughout the white matter. Portions of brain, spinal-cord nerve roots and nerves removed for further examination. A culture in broth from the cerebro-spinal was made, which showed a pure growth of diplo-streptococci.

Heart.—Pale and flabby, all the cavities are dilated. A culture in broth from the heart's blood was made, which showed a pure growth of diplo-streptococci.

Lungs.—Left is adherent throughout the whole extent. The adhesions are fairly easily broken down, and are of fairly recent date; the lung is partially collapsed. The pericardium and heart are partially drawn to the left side. The right lung is normal.

Liver.—Shows a condition of chronic venous congestion.

Spleen.—There is some old perisplenitis and a scar across the organ near its centre. On section the substance is congested and shows old malarial pigmentation.

Kidneys.—Both show early chronic venous congestion.

Glands.—All the groups are enlarged and congested. Both femoral groups show points of suppuration. In the left cervical group near suboccipital triangle a deeply placed gland shows several points of suppuration. A culture was made in broth from a gland in the left cervical region showing no points of suppuration.

Remarks.—This is another very interesting case. Although the gland juice was examined so late as 12 days before death no streptococci were detected, but the juice contained a very large number of active trypanosomes. On post-mortem examination we find not only the femoral group of glands suppurating but also the deeply placed glands in the neck. In this case, therefore, the invasion by the diplococcus was purely terminal, probably it gained entrance through the many suppurating abrasions occasioned by the jiggers. The vitality of the patient also having become greatly lowered, the glands nearest the seat of infection, viz., the femoral and axillary, were unable to deal with the germ, and so it became generalized.

CASE 69. K.P. ARCADİ (MALE). AGE 25 YEARS.

May 17, 1904. The patient lives at the Swahili village, Entebbe. He has been headman to one of the Indian traders at Entebbe. He is at present a prisoner. He states he has been sick for six months. He now presents a dull heavy facial expression. He has slight tremors of the tongue. There is no headache or itching of the skin. The pulse is 100; tension fair. His superficial lymphatic glands are generally enlarged.

May 27. Opened a small abscess at root of toes of left foot. His general condition is unchanged.

June 1. A gland in the left posterior triangle of neck was punctured. The juice contained a large number of active trypanosomes. Some of the juice was planted on a tube of blood agar; this remained sterile. He is in the late second stage of the disease.

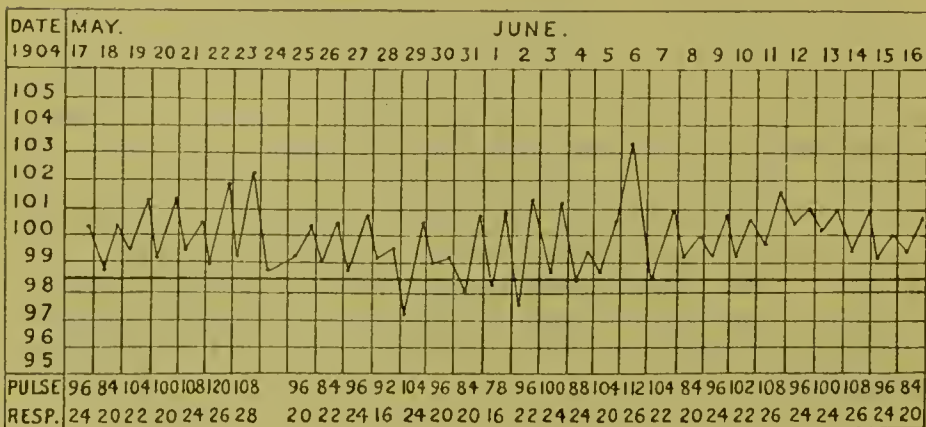
July 14. Patient's condition has deteriorated considerably. He has general tremors of the body, and the facial expression is very dull. A gland in left posterior triangle of neck was punctured, and the juice was seen to contain active trypanosomes in very large numbers. Tubes of broth and agar were inoculated from the juice. Both showed a pure culture of a diplococcus next day.

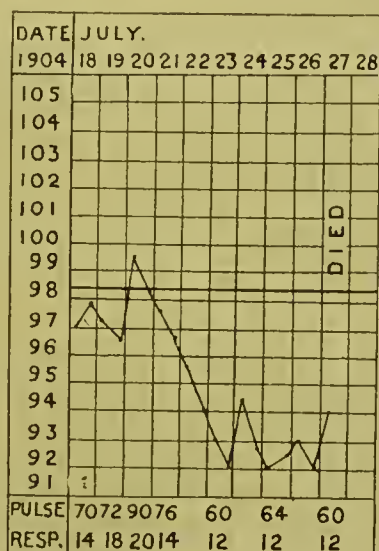
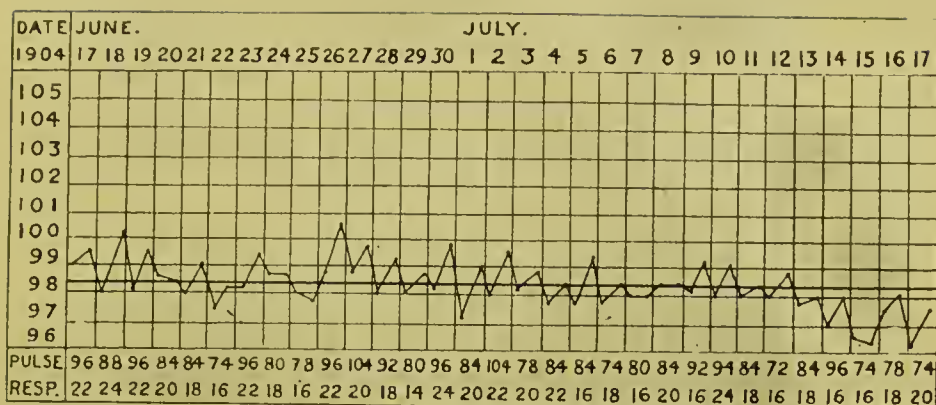
July 15. The tremors are now general, but more marked on the right side of the body. His speech is very indistinct. He does not complain of pain. The knee jerks are both present but somewhat diminished. Ankle clonus is present. Heart sounds are normal, no bruit.

July 19. The patient is now unable to speak. The tremors are well marked. He is considerably emaciated.

July 21. The patient is now practically moribund. Jiggers present in both feet.

The following chart shows the course of the disease:—





The following table shows the result of the enumeration of the blood corpuscles, the percentage of hæmoglobin, the presence or absence of diplococci and trypanosomes in the glands, blood, and cerebro-spinal fluid :—

Date.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in blood.				Parasites in C.S.F.	
			P.N.	S.M.	L.M.	E.		Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.	
1904.															
May 17	...	5,100,000	35	34	29	2	84	-	+	-	-	+	-	+	
June 1	-	+	
July 14	...	6,000,000	46	36	11	7	100	+	+	-	-	+	
" 19	...	6,000,000	55	33	9	3	102	+	+	+	-	+	
" 21	...	6,020,000	50	43	5	2	102	+	
" 27	+	+	+	...	

July 27, 1904. Patient died. Post-mortem.

The body is that of a well-built man. There is considerable emaciation. The pupils are equal and normal. There is general enlargement of superficial lymphatic glands.

There is no increase of fluid in the pericardial, pleural or peritoneal cavities.

Brain.—On removing the calvarium and reflecting the dura mater, the superficial vessels are seen to be infected. There is an increase of the sub-arachnoid fluid, giving a ground glass appearance to the membranes. The ventricles are dilated. The spinal cord presents no noteworthy naked eye change. Portions of nervous system preserved for future examination.

Heart.—All the cavities are dilated; the muscle wall is pale and flabby. There are no petechiæ; a tube of broth inoculated with the blood of this organ showed a pure culture of diplococci.

Lungs.—Both normal.

Liver.—Some fairly recent adhesions between the liver and the diaphragm. The substance shows typical nutmeg condition.

Spleen.—Some fairly recent adhesions and old perisplenitis. On section it is congested, and shows old malarial pigmentation.

Kidneys.—Nothing noteworthy.

Glands.—There is very marked enlargement of the cervical glands, and some of the deep ones in this region showed points of suppuration. The other groups of glands were also markedly enlarged; a tube of broth was inoculated from a gland in the suboccipital region, and showed a pure culture of diplococci.

Stomach.—The mucous membrane presented a curious condition, it was studded with minute hæmorrhagic areas; these areas had a dark centre of altered blood and a peripheral zone of light red; there were also a few larger areas. No ova of *Bilharzia* were seen in the scrapings.

Remarks.—This is an interesting case. It showed during its course a remarkable number of trypanosomes in the glands, blood, and cerebro-spinal fluid. The trypanosomes were found in the cerebro-spinal fluid without centrifuging. Cultures were made from the lymphatic glands on June 1, these remained sterile: very many active trypanosomes were present in the juice. On July 14 cultures made from the lymphatic glands showed a pure culture of diplococci. Here again we had a case with all the classical signs of an advanced stage of the disease at the date of examination of the glands, and although many trypanosomes were present, no diplococci were found. The invasion by diplococci did not occur until the patient was in practically a moribund condition. The number of red blood corpuscles rose before death to 6,020,000 per mm.³, and the percentage of hæmoglobin at the same time rose to 102. The condition of the mucous membrane of the stomach was very interesting in this case.

The following photographs show the enlargement of the lymphatic glands in case of No. 69 ZN. Arcadi on June 5, 1904:—





CASE 237. SEMPAGAMA (MALE). AGE 8 YEARS.

October 29, 1903. Patient admitted to hospital. He lives in Entebbe near the shore of the Lake. He complains of pains all over his body. The patient presents a heavy dull facial expression, and his voice is somewhat weak. There is no tremor of the tongue or fingers. The knee joints are normal. The spleen is slightly enlarged. The pulse is 84. weak. The heart sounds are normal.

December 29. The general condition is now more marked. There are now general tremors of the body.

February 28, 1904. The patient is getting thinner, and generally shows signs of progressive deterioration of health.

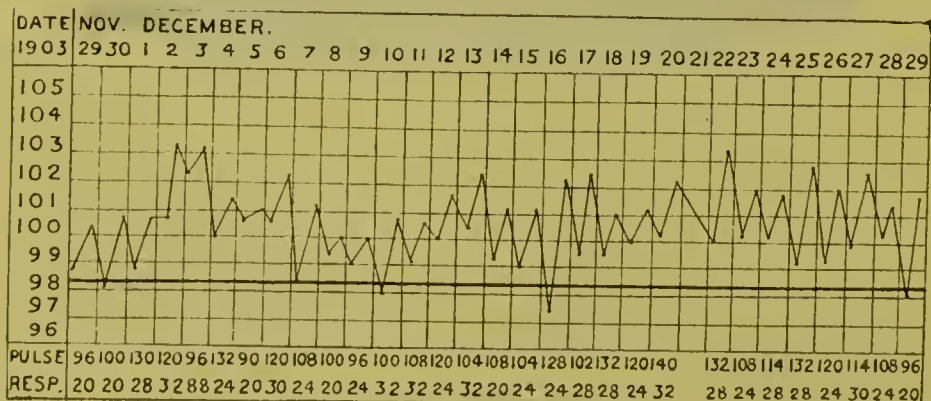
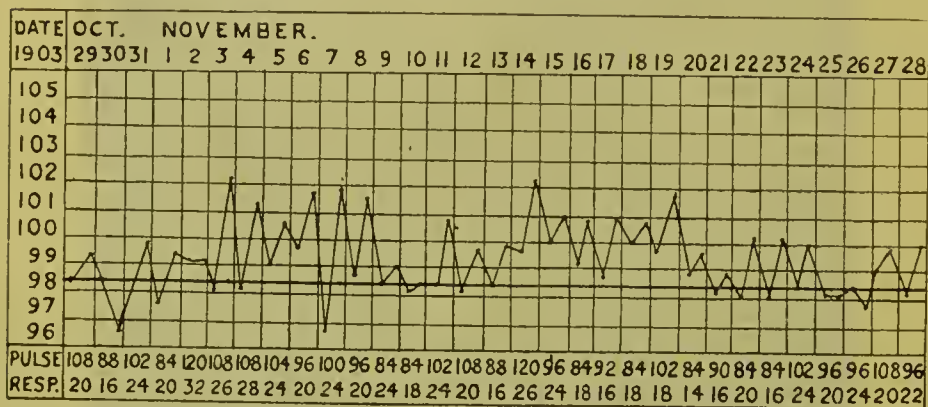
March 2. The glandular enlargement is general, and well marked.

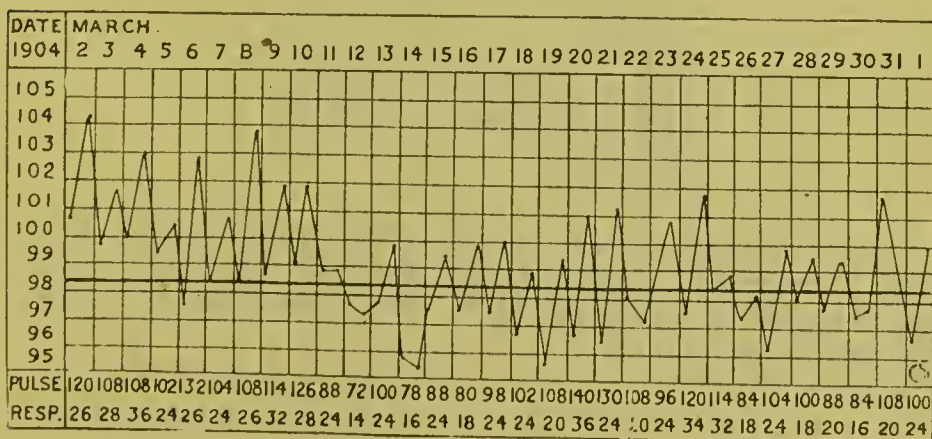
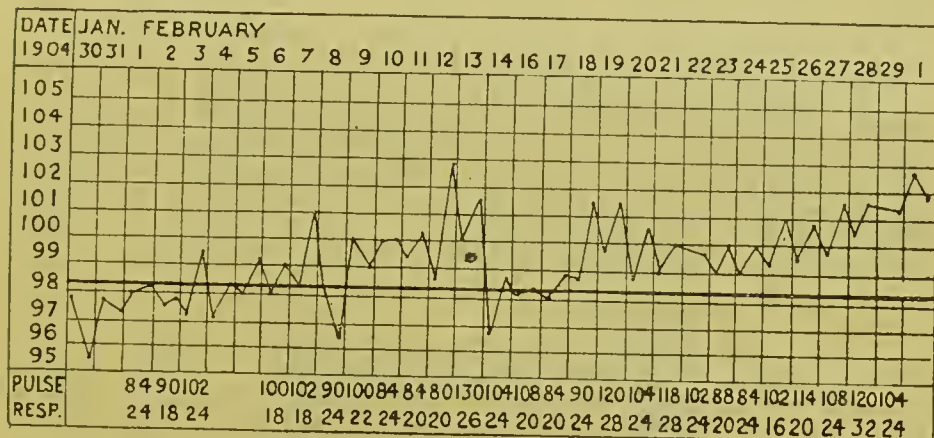
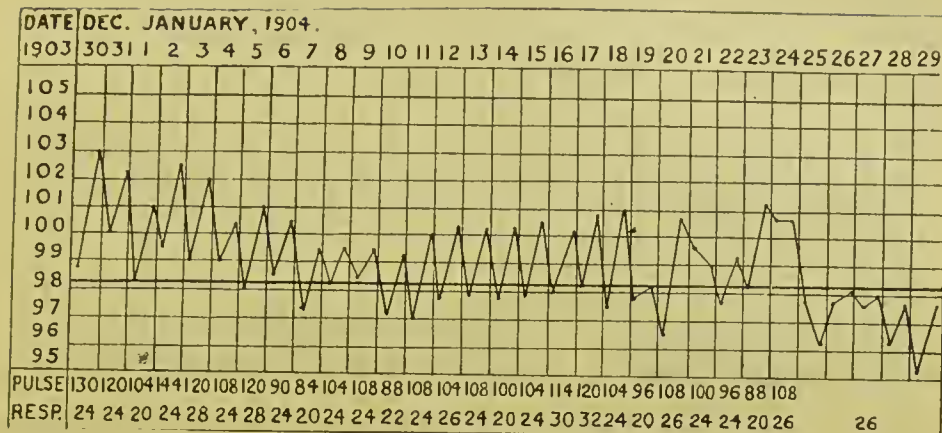
March 14. A gland in the right posterior triangle of the neck was excised.

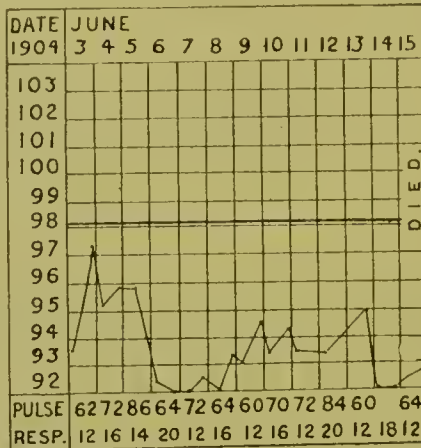
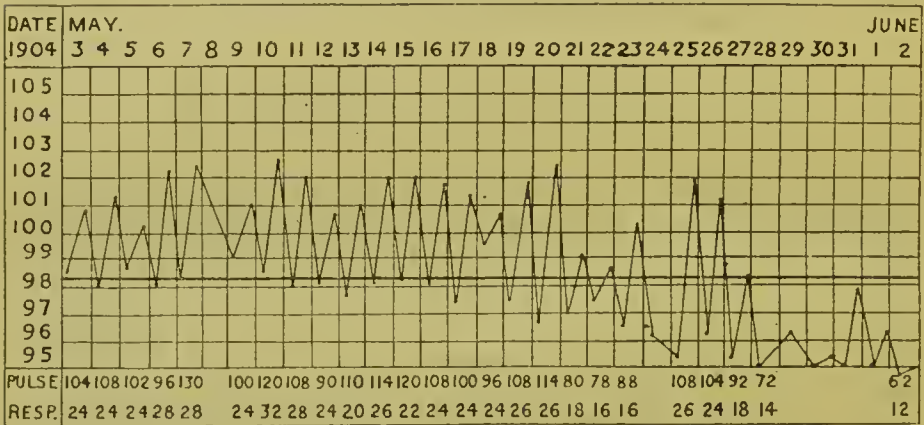
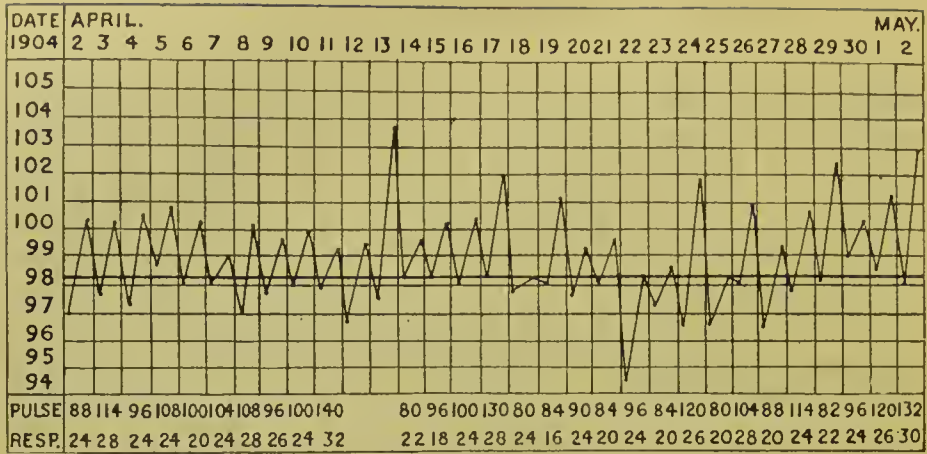
May 27. The patient is now extremely emaciated. He lies doubled up in bed, and is asleep the whole day. The voice is very feeble.

June 5. The patient is reduced to mere skin and bone. The glands in the left posterior triangle of neck were punctured. The juice was examined microscopically, and cultures on agar were made. 10 c.c. cerebro-spinal fluid was placed in broth; it remained sterile.

The following chart shows the course of the disease :—







The following table shows the result of enumeration of the blood corpuscles, and the presence or absence of the trypanosoma and diplococcus in the lymphatic glands, blood and cerebro-spinal fluid.

Date.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.	
			P.N.	S.M.	L.M.	E.		Strept.	Tryp.	Fl.	Mal.	Tryp.	Strept.	Tryp.
1904.														
Oct. 29	+	...	-	+
March 14	-	+	...	-	-
" 16	53	33	14
June 2	...	4,350,000	62	16	11	11	70	-	-	+
" 5	...	4,400,000	33	45	19	3	72	-	+	-	-	+	-	+
" 15	...	3,600,000	42	43	15	0	70	-	+	-	-	+	-	+

June 15. Died at 12.30 p.m. Post-mortem one hour later.

The body is greatly emaciated. The superficial lymphatic glands are generally enlarged. The pupils are equal and normal. There are many jiggers in both feet. There is no increase of fluid in pleural, pericardial or peritoneal cavities.

Brain.—On removing the calvarium and reflecting the dura mater the surface of the left hemisphere, corresponding to the parietal eminence, is seen to be covered with a clot of blood, no fracture of calvarium was present. There is some increase of sub-arachnoid fluid. The pia-mater had the usual ground glass appearance. On section nothing noteworthy was observed. Spinal cord showed nothing noteworthy to the naked eye. Portions of the brain, spinal cord, ganglia and nerves preserved for minute investigation. The cerebro-spinal fluid was examined one hour after death, and contained active trypanosomes.

Heart.—Showed nothing noteworthy. The blood from this organ was examined microscopically and many trypanosomes were present. A culture in broth and agar was made from the heart's blood; these showed a growth of *Bacillus coli communis*.

Lungs.—Some old adhesions over the lower lobe of both lungs, otherwise nothing noteworthy.

Liver.—Appears healthy.

Spleen.—Considerably enlarged; shows old perisplenitis, with thickening of capsule; the substance is pigmented.

Kidneys.—Nothing noteworthy.

Glands.—There is considerable enlargement of the abdominal glands and those in the cervical region. The femoral group were markedly enlarged and showed points of suppuration. The axillary group were also enlarged, but showed no points of suppuration. A culture was made from a group of enlarged glands in the left cervical region in broth; this remained sterile.

Remarks.—This case was a very chronic one. The trypanosomes were present in considerable numbers in the gland juice; they were also seen in films of the peripheral blood. There was a remarkable increase of the total leucocytes before death. No diplocoeci could be determined in the lymph juice *intra vitam* nor in the heart's blood or glands post-mortem. The terminal invasion was in this case *Bacillus coli communis*. This must have occurred during life, as the post-mortem was made within an hour of death.

CASE 69 Z.D. USMANI (MALE). AGE 14 YEARS.

May 25, 1904. Patient comes from Usoga. He has been working as a boy in Entebbe. There are tremors of hands and body generally. He is not able to stand. The lymphatic glands are generally enlarged. Facial expression is markedly dulled. Heart sounds normal. Pulse is 76. Liver and spleen are enlarged. The glands in left posterior triangle were punctured and living trypanosomes obtained. The examination

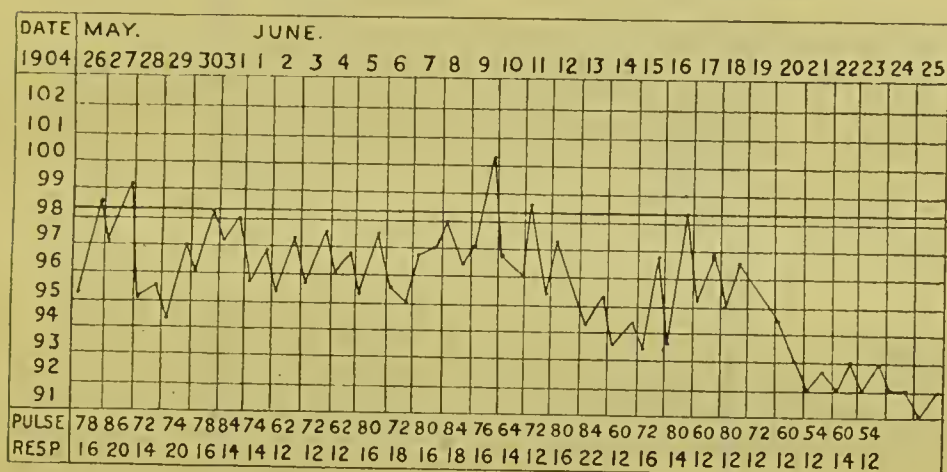
of the cerebro-spinal fluid showed the presence of disintegrating trypanosomes as well as actively motile one. The fluid contained 670 corpuscles per mm.³, all being mono-nuclear.

May 27. The appetite is good. Patient is excited at times and sleeps a good deal.

June 12. The general condition is unchanged. The appetite is good.

June 25. For the last few days patient has shown very marked nervous symptoms. There is general tremor of body. He is practically moribund. The glands in the left posterior triangle of neck punctured; the juice examined microscopically shows diplococci. Culture in broth also shows diplococci.

The following chart shows the course of the disease:—



The following table shows the result of enumeration of the blood corpuscles, the percentage of hæmoglobin and the presence or absence of diplococci and trypanosomes in the blood, lymphatic glands and cerebro-spinal fluid:—

Date.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.	
			P.N.	S.M.	L.M.	E.		Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.
1904.														
May 25	...	4,400,000	28	19	19	34	80	-	+	-	-	-	-	+
June 19	...	5,000,000	33	35	10	22	85	-	+	-	-	-
" 25	...	4,200,000	76	19	4	1	68	+	+	-	-	-	-	+
" 26	+	+	+	...

June 26. Patient died at 12 noon. Post-mortem.

The body is not markedly emaciated. Jiggers in both feet. The pupils are equal and normal.

There is no increase of fluid in the perieardial, pleural or peritoneal cavities.

On removing the calvarium and reflecting the dura mater some flattening of the convolutions is noticed. The sub-arachnoid fluid is increased and the pia arachnoid has the usual ground glass appearance. The superficial vessels are injected. The spinal cord to the naked eye presents nothing noteworthy. Portions of brain, spinal cord, nerve roots, ganglion, nerves and lymphatic glands of neck removed for minute investigation. A culture from the cerebro-spinal fluid shows the presence of a diplococcus.

Heart.—The cavities of both ventricles are dilated. The muscle is pale and flabby. A culture from the blood of this organ shows the presence of diplococci.

Lungs.—The right is very adherent throughout. The left nothing noteworthy.

Liver.—Shows a condition of chronic venous congestion.

Spleen.—Somewhat enlarged and shows chronic venous congestion.

Kidneys.—Both show chronic venous congestion.

Lymphatic glands.—All the groups are markedly enlarged. The femoral group shows points of suppuration. A culture from glands in the left cervical region shows the presence of a diplococcus. Smear preparations of juice show the presence of diplococci and broken down trypanosomes.

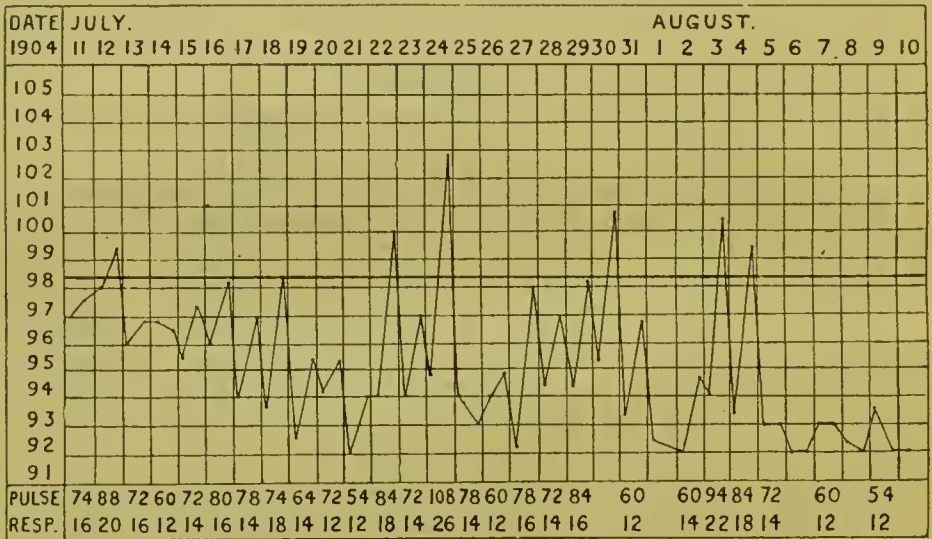
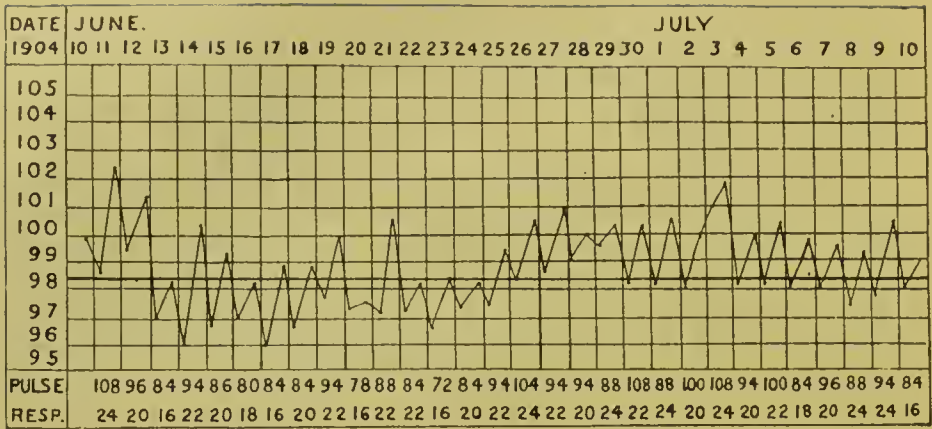
Remarks.—This case is of interest as showing that there was an invasion of the tissues by a diplococcus the day previous to death. The earlier investigation of the glands on June 19, did not show the presence of a diplococcus. Here we have a trypanosome infection with the production of all the signs of the disease. At a later period, practically in the death agony, an invasion of diplococci.

CASE 69 Z.K. MSUBIKA (FEMALE). AGE 7 YEARS.

June 10, 1904. Patient lives on the shore of Lake near Entebbe. She states that she has been ill for one year. She has been sleeping a great deal and complains of pain in the head. She presents a dull facial expression. Choreiform movements of the hands are present. The lymphatic glands are enlarged in the femoral region and groins, slightly in the axillæ and very slightly in the posterior triangles of neck.

August 10. The patient is now in an advanced stage of the disease and is completely bedridden. General tremors of the body are present. Emaciation is not very marked. The spleen was punctured, cultures made in broth, and also smears, which showed under the microscope no fully-formed trypanosomes. The culture remained sterile.

The following chart shows the course of the disease :—



The following table shows the result of the enumeration of the blood corpuscles, the percentage of hæmoglobin, the presence or absence of diplococci and trypanosomes in the blood and cerebro-spinal fluid :—

Date.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.	
			P.N.	S.M.	L.M.	E.		Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.
1904.														
June 10	33	46	13	8	84	-	-	-	-	+
" 22	25	55	8	12	90	-	-	-
Aug. 10	87	10	2	1	90	+	-	-
" 12	+	+	+	...

August 12. Patient died. Post-mortem.

The body is not markedly emaciated. No bedsores. Jiggers in both feet and hands. The superficial glands are generally enlarged.

No increase of fluid in the pleural, pericardial or peritoneal cavities.

Brain.—On removing the calvarium and reflecting the dura mater, the surface of the brain presents the usual appearance of a sleeping sickness case. The subarachnoid fluid is increased, giving a ground glass appearance to the membrane.

The superficial vessels are injected. Portions of the brain and spinal cord removed for minute examination. A culture in broth was made from the cerebro-spinal fluid. A pure culture of diplo-streptococci was obtained.

Heart.—Normal. A culture in broth was made. A pure culture of diplo-streptococci was obtained.

Lungs.—Right is adherent throughout and the lung substance is pale and airless. Left is healthy.

Liver.—Is healthy.

Spleen.—Slightly enlarged, on section it is pigmented.

Kidneys.—Both show lobulation, otherwise nothing noteworthy.

Lymphatic glands.—In groin and femoral region are enlarged. The deep cervical are also enlarged, one in the left subaxillary region showed small points of suppuration. A culture on agar from the gland showed the presence of a diplococcus.

Bone marrow.—Removed from upper end of left humerus. No noteworthy alteration.

Remarks.—This case again shows that the tissues towards to the close of life were invaded by pyogenic cocci.

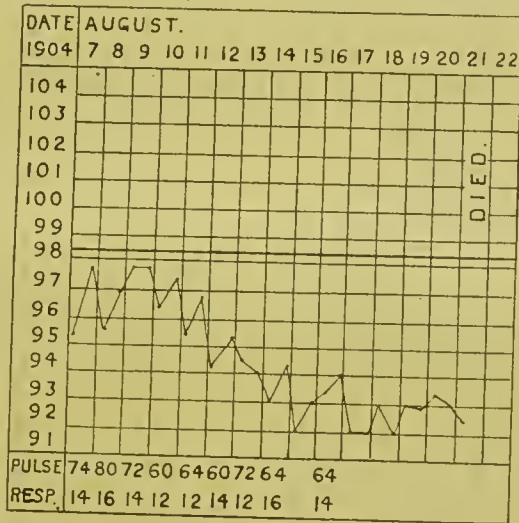
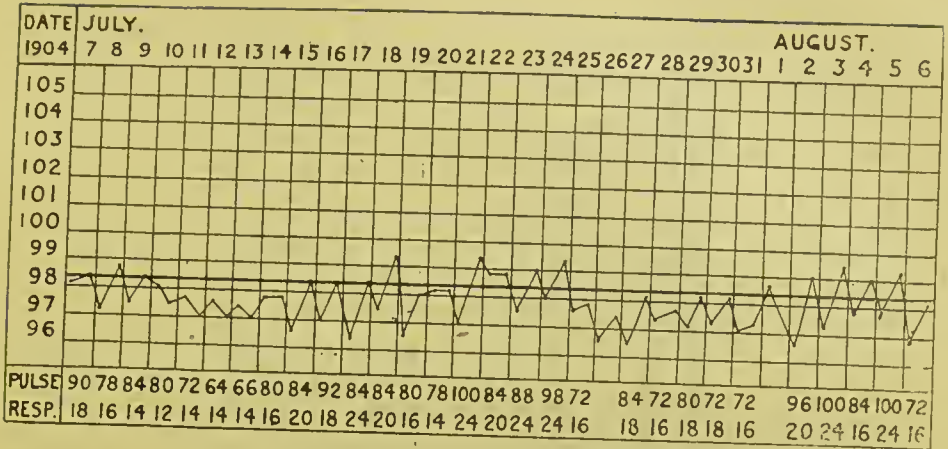
CASE 69 SUEDI (MALE). AGE 35 YEARS.

Z.M.

July 6, 1904. Patient states that he has been sick for 3 months. He suffered from pains all over his body. He now shows a general enlargement of the superficial lymphatic glands. He has now no pains. There are no tremors of tongue or hand. Pulse 134, tension fair. He appears to be in an early stage of the disease. A gland in the left posterior triangle of neck was punctured, active trypanosomes were present, but no streptococci in the juice.

August 18. He has been getting gradually worse and is now unable to walk at all.

The following chart shows the course of the disease:—



The following table shows the result of the enumeration of the blood corpuscles, the percentage of hæmoglobin, and the presence or absence of streptococci and trypanosomes in the glands, blood and cerebro-spinal fluid:—

Date.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in blood.				Parasites in C.S.F.	
			P.N.	S.M.	L.M.	E.		Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.	
1904.															
July 6	...	4,000,000	41	44	8	7	70	-	+	-	-	-	-	+	
Aug. 3	...	4,150,000	55	25	9	11	80	
" 22	+	+	...	

August 22, 1904. Patient died this morning at 4 a.m. Post-mortem.

There are jiggers in both feet. The body is not emaciated. Pupils equal and normal.

There is no increase of fluid in the pericardial, pleural or peritoneal cavities.

Brain.—There is some congestion of the superficial vessels. There is not much increase of sub-arachnoid fluid. The ventricles are not dilated. Spinal cord shows some post-mortem staining of the membranes, otherwise nothing noteworthy. Portions removed for minute examination. A culture on agar was made from the cerebro-spinal fluid.

Heart.—The muscle substance is fairly firm. Both posterior cusps of the aortic valve show a condition of endocarditis; on the right there is a fairly recent vegetation, the left being shrunken, the pulmonary is normal, the tricuspid and mitral valves show nothing noteworthy. A culture on agar was made from the blood of this organ.

Lungs.—Both healthy.

Liver.—Presents a peculiar condition. The right lobe is apparently normal, but to the left of falciform ligament the liver tissue stops abruptly, there being thus no left lobe. The organ is preserved for further investigation.

Spleen.—Slightly enlarged, rather soft, friable on section. On microscopic examination the pulp was seen to contain many diplo-streptococci.

Lymphatic glands.—There is general enlargement of both superficial and deep glands. The deep cervical shows points of suppuration, the pus on microscopic examination contains diplo-streptococci. A culture on agar was made from juice.

Remarks.—In this case there was a general invasion by a diplo-streptococcus before death. There was also a recent endocarditis, probably associated with the general infection. The invasion must have occurred at a stage when the resisting power of the patient was very low and helped the fatal termination.

CASE 69 ZIMAGEZA (MALE). AGE 14 YEARS.

Z.N.

July 11, 1904. Patient was admitted into the hospital on July 4. He lives at Bugabu, near Entebbe, on the shore of the lake. He states he has been ill for six months. He complains of pains all over his body. He now presents all the usual signs of a case of sleeping sickness in the late second stage of the disease. The facial expression is very dull. The voice is weak and monotonous. Tremors of hands and tongue are present. The superficial glands are generally enlarged. The spleen is slightly enlarged. Liver is not enlarged. The heart sounds are weak, no bruit. Pulse 100, tension is low. A gland in the left posterior triangle of neck was punctured; active trypanosomes were present, no streptococci.

July 19. The patient is rapidly deteriorating in his general

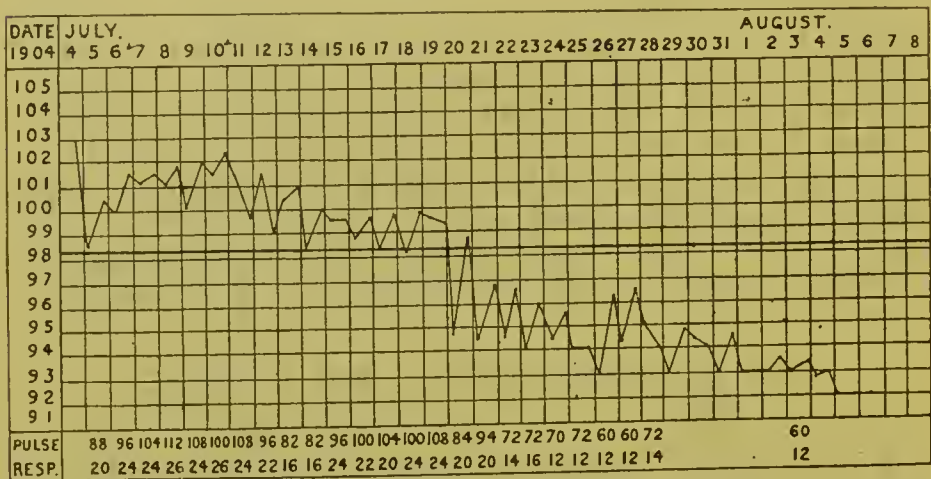
condition and is now practically bedridden being, in the last stage of the disease. A gland in the left posterior triangle was punctured, many active trypanosomes were present. The blood examined by films showed also many trypanosomes. Arsenious acid, 15 milligrammes, was injected into muscle of left gluteal region.

July 20. The glands in left posterior triangle of neck were punctured, no active trypanosomes were present. Examination of the blood by films also showed the absence of trypanosomes. No streptococci in the glands.

July 29. The examination of the blood of this patient showed that there was a marked increase in the number of the red corpuscles and the percentage of hæmoglobin. The specific gravity was 1068. 1.5 litres of 0.75 per cent. sodium chloride solution were injected subcutaneously into both axillæ at 12 noon. The examination of the blood at 3 p.m. on the same day showed that the number of red cells had fallen from 6,400,000 to 5,400,000, and the percentage of hæmoglobin from 100 per cent. to 83 per cent., and the specific gravity from 1,068 to 1,065.

August 5. The patient is now practically moribund. The spleen was punctured. Examination of the blood from the spleen showed no active trypanosomes, but a number of diplococci were present, also a few nucleated red corpuscles.

The following chart shows the course of the disease :—



The following table shows the result of the enumeration of the blood cells, the percentage of hæmoglobin and the presence or absence of trypanosomes and diplococci in the lymphatic glands, blood and cerebro-spinal fluid :—

Date.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.	
			P.N.	S.M.	L.M.	E.		Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.
1904.														
July 11	5,000,000	10,900	52	28	18	2	88	-	+	-	-	+	-	+
" 19, 10 a.m.	5,000,000	11,800	40	46	13	1	90	-	+	-	-	+
" 19, 4 p.m.	54	40	6
" 20
" 21	5,200,000	8,120	30	51	8	11	92	-
" 23
" 26
" 27
" 29	6,400,000
" 29	5,400,000	8,700	100
" 5	83
Aug. 7	+
"	+	+	..

August 7, 1904. Patient died in the night. Post-mortem.

The body is distinctly emaciated. Jiggers in both feet. There are no bed-sores. There is general enlargement of superficial lymphatic glands.

There is no increase of fluid in the pleural, pericardial or peritoneal cavities.

Brain.—There is some increase of sub-arachnoid fluid, giving the usual ground glass appearance to the membranes. The superficial vessels are injected. There is no flattening of the convolutions. The ventricles are dilated. The spinal cord shows no noteworthy change. Portions of brain, spinal cord, nerves with ganglion and roots removed for minute investigation. A culture in broth of the cerebro-spinal fluid shows the presence of a diploeoccus.

Heart.—Cavities are dilated, the muscle wall is pale and flabby, otherwise nothing noteworthy. A considerable number of nucleated red blood corpuscles are present in the blood of this organ. A culture in broth of the heart's blood shows the presence of a diploeoccus.

Lungs.—Left shows some hypostatic congestion towards its posterior aspect and small areas of collapse. The right lung is healthy.

Liver.—Shows a condition of advanced chronic venous congestion.

Spleen.—Is enlarged and congested, a film from this organ shows the presence of a diplococcus.

Kidneys.—Both show early stage of chronic venous congestion.

Intestines.—Normal.

Lymphatic glands.—All the groups are distinctly enlarged and markedly congested. Films made from the glands show the presence of a diploeoccus. A culture in broth from a cervical gland gave a pure culture of diplo-streptococi.

Bone Marrow.—The marrow was removed from the upper end of the right humerus. It presented a somewhat deeper red colour than normal. Film preparations were made and stained. These showed a remarkable increase in the number of nucleated red corpuscles, many were of the normoblastic type, but some, also, were apparently megaloblastic.

Remarks.—This case is of considerable interest and importance. One of the most striking features in it was the remarkable blood picture presented. During life the number of the red cells, the percentage of hæmoglobin and the specific gravity were higher than normal. The blood during life showed nucleated red corpuscles. After death the examination of the bone marrow showed a very large number of nucleated red cells. The changes in the blood took place shortly before death. In this case there was a general invasion by a diplococcus just before death. To what extent this was responsible for the peculiar condition of blood and bone marrow it is difficult to say. At one time this patient had a very large number of trypanosomes in the peripheral blood. The effect of injection of

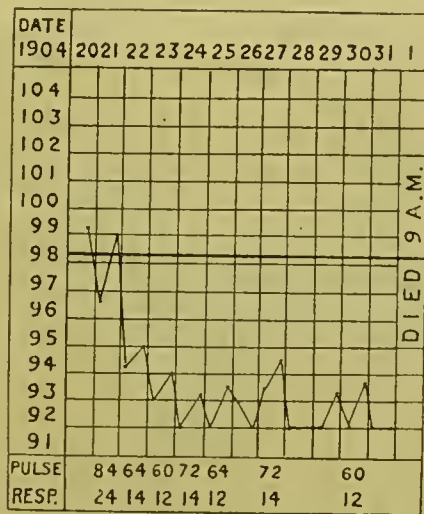
a considerable quantity of salt solution in diminishing the number of red cells, percentage of hæmoglobin and specific gravity (which were all higher than normal) was interesting. The result of the injection of the sodium arsenite was also interesting.

CASE 69 Z.Q. GEERUDE (MALE). AGE 25 YEARS.

August 20, 1904. Patient, who is a Waganda, was sent in from Kakumiro. He complains of pains in his body, and has been sick for some time. He is now very drowsy, and his speech is slow and monotonous. Facial expression is dull. Slight tremors of tongue and hand present. The heart sounds are normal. Pulse 85, tension is fair. Lungs normal. The knee jerks are present and normal. A gland in the right posterior triangle of neck was punctured, and the juice was found to contain active trypanosomes, but no diploeocci. The cerebro-spinal fluid also contained active trypanosomes.

August 30. The patient has been passing black motions for about two to three days. No vomiting.

The following chart shows the course of the disease:—



The following chart shows the presence or absence of trypanosomes or diploeocci in the lymphatic glands and cerebro-spinal fluid:—

Date.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.	
	Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.
1904.							
Aug. 20 ...	—	+	—	—	+	—	+
Sept. 1 ...	—	—	...

September 1. Patient died. Post-mortem.

The body is not emaciated. There is general enlargement of the superficial lymphatic glands.

No increase of fluid in the pericardial, pleural or peritoneal cavities.

Brain.—Shows some congestion of the superficial vessels and increase of sub-arachnoid fluid. The ventricles are dilated. A culture in broth made from the cerebro-spinal fluid remained sterile.

Heart.—Nothing noteworthy. A culture in broth made from the heart blood remained sterile.

Lungs.—Both healthy.

Liver.—Nothing noteworthy.

Spleen.—Slightly enlarged.

Kidneys.—Nothing noteworthy.

Pancreas.—Is somewhat enlarged and congested.

Stomach.—On opening this organ it is found to contain a considerable quantity of altered blood. The mucous membrane is seen to be studded with a large number of areas which have a dark centre and a periphery of lighter red in the centre, the mucous membrane is eroded. These areas vary in size, are circular in shape. Scrapings from these ulcers did not show the presence of ova of *Bilharzia*. *Vide Plate.*

Intestines.—Are normal.

Remarks.—This case is given on account of the curious condition met with, post-mortem, in the stomach; since attention has been directed to this point the stomach of four cases of sleeping sickness have been examined, and a very similar condition found in each. These areas, on microscopic examination are seen to be small hæmorrhages into the mucous membranes, and these become broken down under the action of the gastric juice giving rise to the superficial ulcers.

EXPERIMENT 69 Z.R. ZAKAYO (MALE). AGE 20 YEARS.

August 31, 1904. This patient was admitted into hospital about six months ago. He ran away. He was picked up a few days ago on the road and brought to hospital. He is now in a very advanced stage of the disease. There is considerable emaciation. There is general enlargement of the superficial lymphatic glands. The facial expression is very dull. Tremors of tongue and hands are present. The heart sounds are weak. Pulse 72, tension is low.

Lungs.—No physical signs of disease.

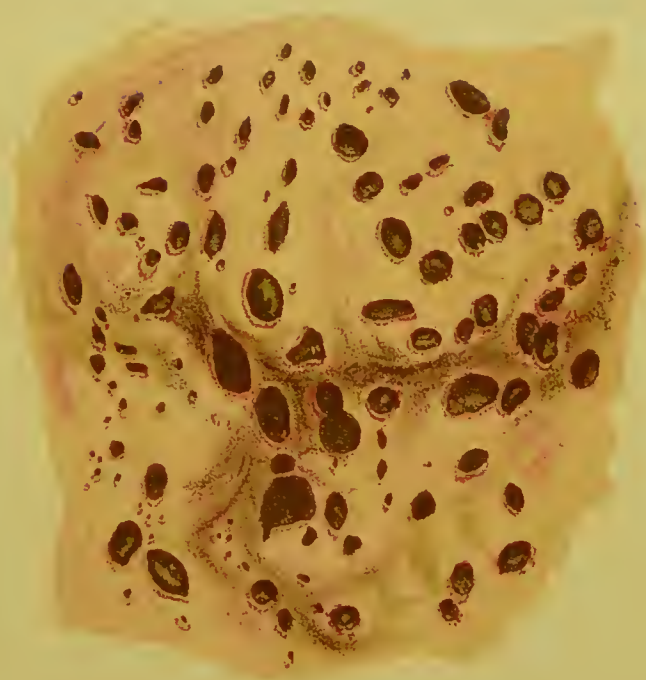
Liver and Spleen.—Are not palpable.

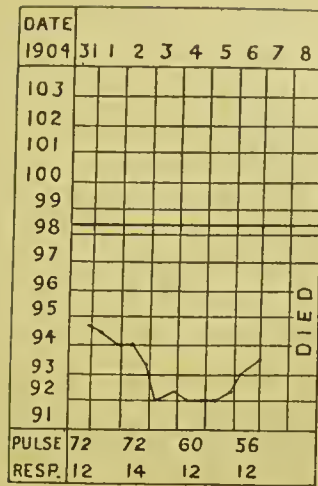
A gland in the left posterior triangle of neck was punctured and active trypanosomes were found in the juice. No streptococci were seen.

September 4. The patient is in a moribund condition.

The following chart represents the course of the disease:—

PORTION OF STOMACH
OF
GEERUDE, CASE OF SLEEPING SICKNESS,
SHOWING ULCERATION OF MUCOUS MEMBRANE.





The following table shows the result of the enumeration of the blood corpuscles, the percentage of hæmoglobin, and the presence or absence of trypanosomes and diplo-streptococci in the glands, blood, and cerebro-spinal fluid :—

Date.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.	
			P.N.	S.M.	L.M.	E.		Strept.	Tryp.	Fil	Mal.	Tryp.	Strept.	Tryp.
1904.														
Aug. 31	-	+	-	+
Sept. 1	...	5,000,000	60	22	12	6	74	-	-
" 8	-	-	...

September 8, 1904. The patient died. Post-mortem.

The body is somewhat emaciated. There is general enlargement of the superficial lymphatic glands. The pupils are equal and normal. There is no increase of fluid in the pericardial, pleural or peritoneal cavities.

Brain.—There is some increase of sub-arachnoid fluid. The membranes have the usual ground glass appearance. The superficial vessels are injected. Spinal cord shows no noteworthy change to the naked eye. A culture in broth from cerebro-spinal fluid examined sterile.

Heart.—Apparently healthy. A culture in broth from heart blood remained sterile.

Lungs.—Both healthy.

Liver.—Not enlarged, has somewhat mottled appearance on section.

Spleen.—Slightly enlarged. Some old perisplenitis.

Kidneys.—Nothing noteworthy.

Stomach.—On opening this organ, the mucous membrane presents a remarkable appearance, there are numerous small petechial areas studded all over its surface, towards the pyloric end they are larger and more numerous. Each area has a dark centre surrounded by a light red zone. They vary in size from about a pin point up to $\frac{1}{8}$ th of an inch in diameter. No ova of *Bilharzia* were seen in the scrapings.

Intestines.—Show nothing noteworthy.

Lymphatic glands.—There is general enlargement of the lymphatic glands. A culture in broth made from the left cervical gland remained sterile.

Remarks.—This case is of considerable interest, owing to the curious condition found, post-mortem, of the mucous membrane of the stomach. This is the fourth case in which the stomach has shown this change in sleeping sickness. It would therefore appear that this morbid condition is in some way bound up with the pathology of the disease.

CASE. KASEMOTE (MALE). AGE 35 YEARS. WANYAMWESI.

August 12, 1904. Patient was sent up for examination. Lymphatic gland in left posterior triangle was punctured and the juice found to contain active trypanosomes. He refused to remain in hospital.

October 1. Patient was admitted to hospital to-day. He is distinctly ill. Superficial lymphatic glands are enlarged generally. Complaints of vomiting, especially after food. His voice is low and monotonous, speech is very indistinct. Facial expression is dull. Tongue is tremulous. Heart sounds are normal. Cerebro-spinal fluid contains many active trypanosomes. They were found without centrifuging.

October 10. General condition of patient is much worse, and he is completely bedridden.

October 17. Patient died.

October 18. Post-mortem. The body is emaciated. No

bedsores, general enlargement of superficial lymphatic glands. Port-mortem, decomposition advanced. No increase of fluid in the pericardial, pleural or peritoneal cavities.

Heart and Lungs.—Both normal.

Spleen.—Very slightly enlarged.

Liver.—Healthy.

Stomach.—Towards the pyloric orifice several small petechial hæmorrhages are present. Also several larger areas of congestion. The appearance is very similar to that found in several other cases of sleeping sickness.

Intestines.—Normal. No ova of Bilharzia found in the stomach or intestines.

Remarks.—This case is given, as it is another example of this curious condition of stomach which has been met with amongst the cases of sleeping sickness here.

CASE. SEBUGWAO (MALE). AGE 19 YEARS.

September 27, 1904. Patient lives in the Swahili lines, Entebbe. He has been sick for two months. He complains of pain in the head. The facial expression is dull and heavy. General enlargement of the superficial glands. Spleen is enlarged. Liver is not enlarged. Heart sounds are normal. Lungs, nothing noteworthy. Gland in the left posterior triangle of neck was punctured, a culture in broth was made from the juice, this remained sterile. The juice contained many active trypanosomes. The cerebro-spinal fluid contained active trypanosomes.

October 31. Patient died.

November 1. Post-mortem.

The organs generally present the usual appearances met with in cases of sleeping sickness. The stomach, however, presents a curious condition. The mucous membrane is studded with petechial areas, and the stomach also contains a quantity of dark material. The condition is very similar to that observed in the other cases of sleeping sickness.

Remarks.—This case is given to again direct attention to the frequency of this peculiar condition of the mucous membrane of the stomach.

CASE 69. ZURURU BIN MZA. AGE 25 YEARS.

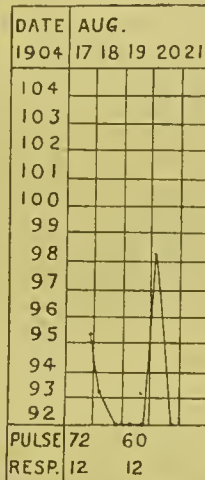
Sailor on Government boat, Lake Albert. Swahili.

August 17, 1904. Admitted to hospital to-day. Captain Hutchinson writes, "That this man was one day in Entebbe before proceeding to Lake Albert, where he remained two years." He was ill for two months on Lake Albert, suffering from pains in the body. He has a very dull, drowsy expression of the face. There is general enlargement of the lymphatic glands, very marked in the anterior and posterior triangles of the neck. Tremors of tongue and hands present. Knee jerks

are normal. Spleen and liver not enlarged. Heart, no bruit heard. His voice is very low and monotonous. He is expectorating rusty sputum. A gland in posterior triangle of neck was punctured, many active trypanosomes present in the juice.

August 18. Lumbar puncture performed. Trypanosomes present without centrifuging. A culture in broth and agar of juice from gland in left posterior triangle remains sterile.

The following chart shows the course of the disease:—



The following table shows the result of enumeration of the blood corpuscles, the percentage of hæmoglobin, the presence or absence of diplo-streptococci and trypanosomes in the blood, lymphatic glands, and cerebro-spinal fluid:—

Date.	R.B.C.	W.B.C.	Percentages.				Hb. per cent.	Parasites in glands.		Parasites in blood.			Parasites in C.S.F.	
			P.N.	S.M.	L.M.	E.		Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.
1904.														
August 17	-	+
" 18 ...	4,900,000	3,800	60	22	12	6	66	...	+	+
" 21	-	-	...

August 21. Patient died. Post-mortem.

The body is fairly well nourished. There is general enlargement of superficial lymphatic glands. No sores. The pupils are equal and normal.

No increase of fluid in the pericardial, pleural or peritoneal cavities.

Brain.—On removing the calvarium and reflecting the dura mater the convolutions are seen to be congested with some flattening. The sub-arachnoid fluid is increased. The spinal cord shows nothing noteworthy to the naked eye. Portions of nervous system removed for minute examination.

Heart.—Muscle substance is pale and flabby, cavities are all dilated.

Lungs.—Left, towards the base there is a patch of pneumonic consolidation in a state of red hepatisation, it involves about half the lower lobe of the lung. There are some flakes of recent pleurisy over this area, rest of lung healthy. Right, nothing noteworthy.

Spleen.—Slightly enlarged.

Liver.—Deeply congested.

Kidneys.—Nothing noteworthy.

Glands.—The various groups show enlargement.

Remarks.—This case is of great importance as indicating that the fly belt on Lake Albert has become infected.

12.

REPORT ON SLEEPING SICKNESS IN THE NILE VALLEY.

BY

CAPTAIN E. D. W. GREIG, I.M.S.

In the Introduction to the Report 9 it was mentioned that Captain Greig left Entebbe for England *via* the Nile; this Report contains the record of his observations on the distribution of sleeping sickness and tsetse fly in the Nile Valley.

About a year ago the exact distribution of *Glossina palpalis* was marked out on Lake Albert for the Commission by Mr. W. Y. Wyndham, then Collector, Wadelai. At that time no report of the presence of sleeping sickness in that district had been received. That the "belt" had become infected was suggested, in the first instance, by a case of sleeping sickness (Case 69, Zururu bin Mza) which was admitted into Entebbe Hospital from Lake Albert on August 17, 1904. This case is recorded in Appendix. Later a report was received by H.M. Acting Commissioner, Mr. George Wilson, C.B., from Mr. T. Grant, Collector, Hoima, stating that a

(7309)

disease resembling sleeping sickness had broken out amongst the inhabitants of Bugungu on the north-eastern shores of Lake Albert. It was therefore of great importance to determine (1) if the disease in Bugungu was sleeping sickness; (2) how far north the disease extended; and (3) the distribution of *G. palpalis* along the Nile banks.

The co-operation of the Government of Egypt having been obtained, it was possible to make observations from Lake Albert down the Nile to Khartoum under specially favourable conditions.

I left Entebbe on November 15, 1904, and proceeded direct to Hoima, arriving there on November 25, 1904. Halting there till December 6, the cases of suspected sleeping sickness from Bugungu, collected there for me by Dr. Pooley, Medical Officer, Hoima, were all carefully examined. From Hoima the march was continued to Butiaba on Lake Albert. From there I proceeded to Bugungu by sailing boat "James Martin." At this point I was met by the Government steam launch and proceeded towards the Victoria Nile, examining on the upward journey the south bank as far as the Murchison Falls and the north bank on the return journey. This occupied four days. Proceeding down the Nile, Wadelai was reached on December 11. Halting here two days some of the general population were examined for trypanosoma infection, and the villages for actual cases of sickness. From Wadelai the journey was continued down the Nile to Nimuli. Halting here for four days, an investigation of a number of the general population for trypanosoma infection was made. From Nimuli the march was continued along the right bank of the Nile to Gondokoro. This was reached on December 27, 1904. At Gondokoro I was joined, on December 30, by Dr. Sheffield Neave, sent by the Egyptian Government to co-operate with me. The gunboat "Abu Klea" was placed at our disposal to investigate the banks of the Nile as far as Bor. From here the journey was continued through the sudd in the post-boat "Amka." Khartoum was reached on January 21, 1905. This completed the investigation.

As it is of extreme importance to ascertain whether *G. palpalis* is present or absent, not only on the banks of the Nile but throughout the whole Sudan; an arrangement was made by which each official of the Sudan Government stationed in the various districts will receive a specimen of the *G. palpalis*, with a memorandum requesting information as to the presence or absence of this fly or flies resembling it (collections to be sent for identification to headquarters), and as to the character of the country, etc., should the fly or one resembling it be found. The results of the investigation on the banks of the Nile are recorded on the two maps which accompany this report, *see* p. 102. The red dots represent the distribution of the *G. palpalis* on the one map and of sleeping sickness on the other. It may be briefly stated that the following facts were ascertained:—

1. The disease on Lake Albert from which the people were dying was undoubtedly sleeping sickness.
2. The disease could be traced, in diminishing severity, along the south and north banks of the Victoria Nile, below the Murchison Falls, and as far north as Wadclai.
3. Examination of the lymphatic glands of the general population of Nimuli showed that the proportion of enlarged cervical glands was low, and the examination of the juice of these glands was negative as regards trypanosomes. No case of sleeping sickness has been recorded here.
4. The distribution of *G. palpalis* coincides with the area of sleeping sickness. It terminates on the Nile banks a little north of the point where the 4th degree cuts the Nile. Here the character of the country begins to alter, open spaces and sparse vegetation giving place to undergrowth and trees.
5. *G. palpalis* was not found on the banks of the Nile in the Sudan.
6. *G. morsitans* has been found in the Bahr-el-Ghazal province. This interesting observation was made by Colonel Griffith, D.S.O., P.V.O., who states "that he found *G. morsitans* in the Bahr-el-Ghazal province on the banks of the Pongo River, where the road to Deim Zubeir crosses it."

1. *Sleeping Sickness is present in the "Fly belt" at Bugungu, Lake Albert.*

Eighteen cases were collected at Hoima by Dr. Pooley from Mwanga's shamba, Bugungu.

These were, clinically, typical cases of sleeping sickness at different stages of the disease. Trypanosomes were found in the gland fluid of every case. The cerebro-spinal fluid was examined in several cases and the trypanosomes found in every case. Dr. Pooley reported on December 13, "that six of the above cases had since died."

It is interesting to note that a blood-sucking maggot is found in Unyoro. Specimens were brought in to Dr. Pooley by the natives. Specimens of the maggot have been sent to Mr. Austen for identification. A curious feature was, that the dogs in the sleeping sickness area died in considerable numbers of a wasting disease. Two sick dogs were sent to Entebbe to be kept under observation. Lieutenant Gray, R.A.M.C., writes on January 19, 1905, "that one of the dogs shows trypanosomes. Of the two monkeys and the guinea-pig which we infected from this dog, (a) the guinea-pig has not yet shown trypanosomes; (b) monkey showed trypanosomes eleven days after infection; (c) second monkey has not yet shown trypanosomes." It will remain to be seen from further observation to what variety of trypanosoma this belongs.

2. *Sleeping Sickness is present in the "Fly belt" as far north as Wadelai.*

At various villages on the south and north banks of the Victoria Nile and the right bank of the Nile to Wadelai the general population were examined and the chiefs questioned regarding the occurrence of sleeping sickness. The method of investigation was by examination of the lymphatic glands as recorded in the Report, page 275.

The following table shows the village or station examined, and the presence or absence of sleeping sickness in the general population :—

Name of village or station.	Situation.	Sleeping sickness.	Number of cases.
Borigi ...	South bank, Victoria Nile, 15 miles from mouth.	Present ...	Two early cases.
Fajao ...	Near Murchison Falls.	,, ...	One case reported.
Kimori ...	North bank of Victoria Nile, 7 miles from mouth.	,, ...	Sixteen men examined. Thirteen had enlarged cervical glands with rapid pulse. Chief reports eight persons died in his village last month of sleeping sickness.
Wadelai ...	Right bank Nile...	,, ...	Fifteen of the general population examined. Four had enlarged cervical glands. Trypanosomes found in one. One case of undoubted sleeping sickness.

3. *Sleeping Sickness at the present time does not occur as far north as Nimuli.*

At this station the cervical glands of eighty-seven males of the general population were examined, namely, sixty Nubian Askaris and twenty-seven Askaris from Afuddu. A few of these showed slight enlargement of the cervical glands, but microscopic examination of the juice was negative as regards trypanosomes.

Through the courtesy of Commandant H. V. Calseyde, I was enabled to examine a number of the general population of Dufie in the Enclave. One case of trypanosoma infection was found. This was imported from the interior. This observation

is of considerable importance as indicating a route along which the infection might enter the "Fly belt" of the Nile.

No cases of sleeping sickness have occurred at Gondokoro or in the Sudan.

4. *Glossina palpalis* extends along the banks of the Nile 30 to 50 miles north of the point where the 4th degree cuts the Nile.

The red dots on the map indicate the position where the *G. palpalis* was actually found; at some points it was extremely numerous; this was especially so at Fajao, on both sides of the Nile at the Falls. *G. palpalis* is found all along the banks of the Nile in Uganda territory. It only ceases to occur a short distance south of Gondokoro. It is interesting to note that, at the point where the fly ceases, the character of the country alters completely. It becomes more open, the undergrowth is not found, and the trees are further apart, and therefore affording much less shelter from the sun.

5. *Glossina palpalis* was not found on the banks of the Nile between Gondokoro and Khartoum in the Sudan.

I examined both banks of the Nile at each possible landing place as far as Bor, but with negative results. From Bor the journey was continued through the sudd. No specimen of *G. palpalis* was found, nor at any point on the journey to Khartoum. Dr. Sheffield Neave will continue and extend the observations on these lines in the Sudan under the direction of Dr. A. Balfour.

6. *Glossina morsitans* occurs in the Bahr-el-Ghazal province of the Sudan.

The observation of Colonel Griffith shows that the *G. morsitans* exists on the banks of the Pongo River.* Mr. Brown, of the Imperial Institute, who has recently been in the Bahr-el-Ghazal, considers "that the Fly is more numerous on the west bank. There is a forest of trees on the west bank. The trees are more scattered on the east." He also states "that the Fly occurs on the Jur River near Wau." It is of great importance that this belt should be accurately defined. Dr. A. Balfour, Director of the Gordon College Laboratory, Khartoum, has found trypanosomes in the blood of animals from the Bahr-el-Ghazal.

7. Has the Nile "Fly belt" become infected from Uganda or the Congo?

It is obvious that the infection must have been carried in from one or other of these areas of sleeping sickness. Its

* Vide Map of Africa showing distribution of Tsetse flies by Mr. Austen p. 282.

greater severity in Unyoro and gradual diminution north appears to suggest that it gained an entrance from the Uganda side, but eases are found in close proximity on the left bank of the Nile. It is impossible therefore to definitely answer the question.

The general situation as regards sleeping sickness in the Nile Valley is, that sleeping sickness is slowly spreading in the "Fly belt" and will extend to its northern and southern limit. As the northern limit does not extend into the Sudan, there will not be a direct extension of the disease along the Nile into this country. As, however, a closely related species (*Glossina morsitans*) exists in the Bahr-el-Ghazal province, it will be of the utmost importance to prevent the introduction of people from sleeping sickness areas into this "belt," and to accurately define the limits of the "belt."

I desire to express my most sincere thanks to H.E. Lord Cromer, for enabling me to undertake the investigation in the Sudan: to Sir Reginald Wingate, Sirdar and Governor-General of the Sudan, for facilitating my work in every way, to Colonel Griffith, D.S.O., P.V.O., and Dr. A. Balfour, for information received, and to other officials in the Sudan and Egypt, who helped me in the work, for their constant and generous co-operation. To Mr. George Wilson, C.B., H.M. Acting Commissioner, Uganda, for giving facilities for the work in Uganda; Dr. R. U. Moffat, C.M.G., for help and advice; Mr. T. Grant, Collector, and Dr. G. H. Pooley, M.O., Hoima; Mr. P. W. Cooper, Collector, and Dr. G. C. Strathairn, M.O., Wadelai; Mr. Guy Eden, Collector, and Dr. Ralph Stoney, M.O., Nimuli; Mr. F. Spire, and Dr. C. J. Baker, M.O., Gondokoro, for help and co-operation whilst on tour in Uganda.

13.

THE DISTRIBUTION OF THE TSETSE-FLIES.

(Genus *Glossina*, Wiedemann, as at present known.)

WITH MAP.

BY E. E. AUSTEN, F.Z.S.

(Author of *A Monograph of the Tsetse-flies*, etc., etc.)

ALTHOUGH our knowledge of the distribution of the eight species of tsetse-flies is still very far from complete, it is nevertheless possible, owing in large measure to the special attention that has been paid to the genus *Glossina* within the last two years, to make an attempt to illustrate the distribution of the various species by means of a map. In view of the possibility that the trypanosome of sleeping sickness may be conveyed by other species of *Glossina* besides *Gl. palpalis*, it is

the more important that this should be done, especially since no such attempt has hitherto been made. The map published in the writer's Monograph of the Tsetse-flies (1903) merely showed what was then known of the distribution of the genus as a whole, without attempting to discriminate between the species; and although a map showing the distribution of the different species was exhibited by the author at Oxford in July, 1904, in connection with a paper on tsetse-flies* read by him in the section of Tropical Diseases, at the Annual Meeting of the British Medical Association, it was unfortunately not found possible to reproduce the map when the paper was printed. The accompanying map, in the preparation of which the writer has been most kindly assisted by Mr. A. J. Engel Terzi, will, it is hoped, at least serve as a basis for future work.

Since it may now be assumed to be well understood that tsetse-flies are not met with continuously throughout broad tracts of country, but are confined to relatively narrow "belts," which are frequently discontinuous, and are usually to be found along the margins of water-courses, rivers, and lakes, it is perhaps hardly necessary to explain that a particular species must not be supposed to occur everywhere within the areas marked on the map. The latter only shows broadly what is at present known of the *relative distribution* of the different species, which, in view of the scale used, was all that was possible. Similarly, where a species of tsetse is shown as occurring along a river or on the margin of a lake, the map must not be taken as giving any indication whatever of the distance from the water to which the fly is to be found, which in some cases may be merely a few yards.† Moreover, the fact that any particular locality lies within the limits of the occurrence of a species of tsetse, as shown on the map, is not to be taken as implying that the fly necessarily exists there to-day. The areas marked are in accordance with records or the localities of actual specimens, but in some instances, as has certainly happened in the case of *Gl. morsitans* in parts of the Zambesi Valley, owing to the retreat of big game or other causes, tsetse-flies are no longer to be found in places formerly infested by them. When isolated areas are marked as the home of one or more species, it is to be understood that specimens have been received from these localities, or else that there are apparently reliable records of the occurrence there of the species concerned; in many cases more complete collections or fuller information would doubtless prove their existence in intervening localities also.

With these introductory remarks the map may be left to explain itself, but the following notes on certain of the species of *Glossina* will perhaps be of interest.

Glossina palpalis. Rob.-Desv.—This species has recently

* "Supplementary Notes on the Tsetse-flies (Genus *Glossina*, Wiedemann)," by Ernest E. Austen, *British Medical Journal*, Sept. 17th, 1904.

† For information as to "fly-belts," and their extent, and the distribution and limits of Tsetse within these areas, cf. "Monograph of the Tsetse-flies," p. 9, *et seq.*

been reported by Laveran* as occurring at Sengaleam, in Senegal, about six miles from Rufisque, and thirty from Cape Verde; this is the most northerly locality yet recorded for any tsetse-fly. In West Africa the limit of the range of *Gl. palpalis* towards the interior is entirely unknown, so that no attention should be paid to the inner boundary of the area shown on the map. In this region most of the specimens and records of occurrences are derived from localities near the coast, and it is consequently impossible to say how far the species extends into the interior, although it may reasonably be supposed to occur throughout the valleys and basins of the majority of the rivers that fall into the Atlantic within the limits of the tropics. Since we now have records of the occurrence of *Gl. palpalis* at various points between Sengaleam and the Congo inclusive, the species is shown on the map as occurring throughout this area, for, although the evidence is not yet complete, there is no reason whatever to imagine that it will not ultimately be found to exist in all suitable localities within these limits. According to our present knowledge, therefore, the distribution of *Gl. palpalis* extends from Cape Verde in the north-west throughout West Africa to an unknown distance into the interior, and southwards to the Congo. In the equatorial region the eastern limits of the species as at present known are the River Omo, which falls into the northern end of Lake Rudolf, and the eastern shore of Lake Victoria. It was encountered by Dr. Brumpt from the sources of the Welle to the mouth of the Congo, and since Laveran† states that he has identified it among specimens from Katanga, in the south-east corner of the Congo Free State (the most southerly record at the present time), it is probably to be found throughout the Lualaba-Congo system as well. South of the Congo *Gl. palpalis* doubtless occurs throughout the greater part, if not the whole of Portuguese West Africa, since, although actual records of the occurrence of the fly are at present lacking, and no collections have as yet been made in this region, according to Dr. H. Rey,‡ Sleeping Sickness has been observed from Benguela northwards.§

Glossina morsitans, Westw.—In the paper already referred to, Dr. Laveran records the identification by him of this species among material from French Guinea, the Rivers Assinie and Comoë (Ivory Coast), and Katanga in the Congo Free State, to

* *Comptes Rendus des séances de l'Académie des Sciences*, t. cxxxix (Séance du 31 Octobre, 1904), p. 659.

† *Loc. cit.*, p. 662.

‡ Quoted by Christy, Reports of the Sleeping Sickness Commission, No. III, Nov., 1903, p. 7.

§ Since these notes and the accompanying map were prepared, the British Museum has received from Dr. F. Creighton Wellman a form of *Gl. palpalis* taken by him in November last on the Katumbela River, Benguela; the specimens are somewhat different from the typical form, and represent a new sub-species, which the author has described as *Gl. palpalis wellmani*. In the Congo Free State, according to information furnished by the Rev. W. Holman Bentley, of the Baptist Missionary Society, *Gl. palpalis* is abundant some eighty miles to the south-east of Luttete.

the south-west of Lake Mweru. Collections received at the British Museum last autumn from Mr. Robert Codrington, Administrator of North-Eastern Rhodesia, show that *Gl. morsitans* may be said to be distributed throughout North-Eastern Rhodesia.

As regards *Gl. morsitans* in the Bahr-el-Ghazal province of the Sudan, the locality shown on the map is that of the specimen obtained by Colonel Griffiths in 1903, on the Pongo River, between Wau and Dem Zibehr, where the species appears to be very abundant. Dr. Andrew Balfour, of the Gordon College Laboratories, Khartoum, in a letter to the writer dated January 9th, 1904, said that during a recent journey to Uganda a native officer informed him that the fly is found six miles inland from Shambe, on the Bahr-el-Jebel. Dr. Balfour is inclined to think that in the Egyptian Sudan *Gl. morsitans* is "limited to the Bahr-el-Ghazal province, and does not extend further north than the river of that name." Major Penton, R.A.M.C., whom the writer has lately seen, is disposed, as the result of experience gained during recent service with the Egyptian Army, to agree with Dr. Balfour, and thinks that at any rate *Glossina morsitans* is not to be found to the north of Fashoda.

Glossina tachinoides, Westw.—This species is recorded by Laveran* from the river Bani, a tributary of the Niger, in the French Sudan. The same author (*ibid.*, p. 659) also speaks of its occurrence on the Lower Rio Nunez, French Guinea; but, since this is an isolated record, it is not shown on the map.

Glossina pallidipes, Austen.—In October, 1904, specimens of this species were forwarded from Gosha, Jubaland, East Africa Protectorate, by Major L. H. R. Pope-Hennessy, 3rd King's African Rifles. Writing from Kismayu on October 11th last, Major Pope-Hennessy states that the natives say that this fly is deadly to cattle and camels, and adds that "should recruits with the germ of sleeping sickness in them be obtained from Uganda, and be bitten by this fly, the disease may be propagated in Gosha, and perhaps annihilate our only hard-working section of the inhabitants. Apart from questions of humanity, this would put an end to any opening-up of the country."

Glossina longipalpis, Wied.—A specimen of this species obtained long ago by Sir John Kirk and labelled "Zambesi" is in the British Museum collection, but since the precise locality is unknown, the species is not shown on the map as occurring in the region in question. It is recorded by Laveran† from French Guinea and Katanga, Congo Free State.

Glossina fusca, Walk., is now known from a number of widely distant localities, and its area of distribution, in addition to being in all probability co-extensive with that of *Gl. palpalis* in West Africa, also extends to Central and East Africa. Apart from previous records, the writer has recently seen a specimen

* *Loc. cit.*, p. 661.

† *Loc. cit.*, pp. 659, 662.

from Usagara, German East Africa, obtained by the Rev. A. North Wood, in 1904. A specimen in the British Museum collected by Sir John Kirk, is simply labelled "Zambesi," but the occurrence is not recorded on the map for the reason stated above in the case of *Gl. longipalpis*. As regards West Africa, the latest record is one by Laveran (*loc. cit.*) from French Guinea.

Glossina fusca was met with in July, 1904, fifteen miles north-east of Chiromo, British Central Africa, by Major F. B. Pearce, Deputy Commissioner, British Central Africa Protectorate. Writing from "The Residency, Zomba, British Central Africa," on November 8th, 1904, Major Pearce says:—"I have arranged to have a few head of cattle kept within the fly (*Glossina fusca*) zone, so as to arrive at some conclusion with regard to the question whether *Gl. fusca* is dangerous to live stock. In this connection you may perhaps be interested to know that a herd of Government cattle has been kept for years at Chiromo, and it is not an unusual occurrence for them to graze in the Elephant Marsh actually in sight of buffalo. The Chiromo cattle have always done very well, and none have ever been lost from "fly" sickness. The same may also be said concerning the cattle of the chief Makwira, who has a large number of cattle, which always graze in the "Marsh," where buffalo are common. If therefore the only species of "fly" in the Elephant Marsh game reserve is *Gl. fusca*, it would seem that that species is not dangerous to live stock." It may be noted that Major Pearce's statements as to the apparent harmlessness of *Glossina fusca* to domestic animals are supported by Stuhlmann's observations on the same species near Dar-es-Salâm.*

BRITISH MUSEUM (NATURAL HISTORY),
CROMWELL ROAD,
LONDON, S.W.

March 2nd, 1905.

14.








THE MULTIPLICATION OF *TRYPANOSOMA GAMBIENSE* IN THE ALIMENTARY CANAL OF *GLOSSINA PALPALIS*.

BY LIEUTENANT A. C. H. GRAY, R.A.M.C., AND LIEUTENANT
F. M. G. TULLOCH, R.A.M.C.

1. *Can the trypanosome of sleeping sickness multiply in the stomach of Glossina palpalis?*

The following is an outline of the experiments done to prove this. The flies used were brought in daily from the lake shore at Entebbe. It appeared that a dry atmosphere affected the

* Cf. Austen, "Monograph of the Tsetse-flies," p. 300.

-  *Glossina tachinoides*.
-  *Glossina palpalis*.
-  *Glossina longipennis*.
-  *Glossina morsitans*.
-  *Glossina fusca*.
-  *Glossina pallidipes*.
-  Areas where two or more species have actually been found.



vitality of the caged flies, and also had a marked effect on the length of time during which the trypanosomes survived inside them. To counteract this the flies, from the time they were brought in, were kept in cages, placed on a bed of absorbent paper, constantly saturated with water from a reservoir with a syphon attachment.

The flies were kept either 24 or 48 hours after they were brought in. They were then fed on monkeys infected from the cerebro-spinal fluid of sleeping sickness cases. These monkeys showed trypanosomes in varying numbers in a blood film, though never more than one trypanosome to six fields of a 2 mm. objective. Forty-eight hours later they were fed on a fresh normal monkey "A"; forty-eight hours later they were fed on another fresh monkey "B"; forty-eight hours later on monkey "C," and so on. This interval was selected, because from previous trials it seemed a natural one for the fly, and nearly all the flies would re-feed after 48 hours.

An enormous increase occurs sometimes in the number of trypanosomes taken in by the fly, so much so, that the blood in the intestine of the fly literally swarms with them. In this case the appearance of a fresh preparation can only be compared to a similar one made from the blood of a rat dying of Nagana, when the number of parasites equals that of red corpuscles.

This increase was first seen in flies 96 and 120 hours after infection, and was thought to occur first at these periods. Later on it was found that the same increase occurred, and that the same enormous numbers of trypanosomes were found 24 hours after the fly had fed on the infected animal.

When these flies were re-fed in the way described, each successive feed of blood seemed to act as a fresh supply of culture medium, and we have found these greatly increased numbers maintained up to 288 hours (12 days) after the infective feed. It is very probable, therefore, that the increase first found at 96 and 120 hours after infection was only the continuation of one which had occurred in the first 24 hours. After it had been found that this increase could occur in the first 24 hours, observations were made on two monkeys. When examined 24 hours after feeding this multiplication was observed in a total 10 per cent. of all the flies.

On some days a considerable number of flies would be examined, and the increase would not be found in any of them, though they were kept under the same conditions and fed on the same monkey, and though there was no perceptible difference, either in numbers or in morphology, of the trypanosomes as seen in a blood film. For instance, of the flies which fed on Monkey 350 on March 23rd, 5 out of 15 showed this great increase when examined 24 hours later. On the next day the increase was not seen in any of 29 flies examined. On the next day 18 negative flies were examined, and on the day following 10. Three days later, when another box of flies fed on the same monkey was examined, the increase was found in 2 out of 9 flies examined. This increase, which is found in 10 per cent. of flies

24 hours after feeding, is continued at later periods up to 288 hours, in a total of 5.6 per cent. of them. Probably if a much larger number of flies could be fed and examined, it would be found that the increase was continued in the same proportion of flies as showed it originally.

The proportion of male flies brought in is very much greater than that of females. This increase has, however, been observed in one female fly.

2. *What proportion of freshly-caught flies in the neighbourhood of Entebbe contain trypanosomes?*

The following method was used in order to try and find this out:—The flies were kept for 24 hours after they came in. They were then fed on an uninfected normal monkey. Twenty-four hours later they were dissected and examined for trypanosomes. Out of 200 flies examined up to the present, two contained in their intestines the same enormous numbers of trypanosomes as were found in 10 per cent. of flies which had been fed on an infected monkey 24 hours previously.

3. *Morphology of the trypanosomes seen in the fly.*

The forms of trypanosome seen in the fly vary from very small ones, some 20μ in length, to very long slender ones of about 100μ . The most striking variation from the ordinary form seen in the blood, however, is the different position of the micronucleus. This is very rarely seen at the extreme blunted end of the parasite. It varies from a position midway between the posterior extremity of the trypanosome and the macronucleus, to a position on the anterior or flagellar side, Figs. 1 and 2. In trypanosomes from the fly the most common positions for the micronucleus are, either anterior to the macronucleus or at the side of it. A very common dividing form is that seen in Fig. 3, which would give rise to two trypanosomes, one with an anterior micronucleus and the other with a micronucleus at the side of the macronucleus. The very small forms have been observed to be produced by unequal division of a large trypanosome, as in Fig. 4. No vacuole is seen in any of these trypanosomes. The blue-staining granules in the protoplasm are present as in the ordinary forms from the blood. What seems their natural method of progression is with the flagellum foremost. They then move very rapidly along a straight course, with only the flagellum and undulating membrane vibrating, the rest of the trypanosome having no lateral movement at all. They can also move with the blunt posterior extremity first, but in this case they move very slowly; their path is zig-zag instead of straight, and they advance by a series of contractions which bend one-half of their body at right-angles to the other. With greatly increased numbers of trypanosomes in a fly at any period after infection there is, in most cases, a large proportion of forms with



FIG. 1.



FIG. 2.



FIG. 3.



FIG. 4.

- FIG. 1a. Trypanosome with micro-nucleus half way between blunted extremity and nucleus.
 FIG. 1b. Trypanosome with micro-nucleus at side of nucleus.
 FIG. 2. Forms with anterior micro-nuclei.
 FIG. 3. Common dividing form.
 FIG. 4. "Budding off" of one of the smallest forms.

anterior micronucleus. In some cases, however, all the trypanosomes found in a fly are practically normal in appearance, the micronucleus being near the posterior extremity. Of the two "fresh" flies which contained trypanosomes, one contained forms almost all of which had an anterior micronucleus, the other showed almost "normal" trypanosomes. Rosettes of trypanosomes have been seen in both fresh and stained preparations. In these rosettes the trypanosomes are joined directly by their posterior extremities; there is no central mass of protoplasm. They vary from very distinct rosettes of 4 to 7 trypanosomes to large loosely woven masses of 15 to 20, most of which are joined at their extremities, but some of which, either naturally, or in making the preparation, are a little separated and lie entangled among the others. When observed in a fresh preparation these rosettes become smaller from breaking away of some of the individuals; there is nothing in the nature of agglutination. In some rosettes every trypanosome belonged to the type in which the micronucleus is anterior. Other rosettes were composed of forms with the micronucleus either at the side of the nucleus or touching it posteriorly. One stained preparation showed a mass of trypanosomes visible with a hand lens. It consisted of a long strip of trypanosomes lying side by side, closely opposed to each other, and four or five deep. It had the appearance of a mass or colony formed by progressive multiplication. Several oval forms of trypanosome have been observed with a darkly staining blue protoplasm, macro- and a micronucleus. These oval forms frequently have a capsulated appearance, possibly due to the remains of the flagellum. In the examination of these flies the whole gut was dissected out in each case, and its various parts mixed with normal saline examined fresh. If examined soon after re-feeding the fly, the trypanosomes are confined to the dark, altered blood in the lower gut, but later on they swarm throughout the blood in the whole alimentary tract. As in the case with cerebro-spinal fluid or gland juice, the medium surrounding the trypanosomes in the fly was found to hinder staining of the chromatin. Accordingly films were made and fixed while still wet in osmic vapour. They were then treated with an application of fresh blood serum, as recommended by Lieut.-Colonel Leishman for sections containing trypanosomes. This was then washed off and they were stained by Leishman's stain. This method gives a very clear staining of the chromatin elements, and they are not obscured by the granules in the protoplasm, which stain a deep blue.

4. *Can infection be conveyed to an animal by inoculating these trypanosomes from the intestine of the fly?*

The following experiments have been done in connection with this point: Monkey 380 was injected with the intestinal contents of a fly which had been fed on an infected monkey 120 hours previously and re-fed in the usual way. This fly

contained enormous numbers of trypanosomes. The monkey was frequently examined, but never found infected. 49 days later the contents of 10 flies, which had fed 24 hours previously, were ejected. A drop of the fluid injected showed numerous active trypanosomes, but the monkey remained uninfected. Monkey 381 was inoculated with the contents of 20 flies which had been infected 96 hours previously (and re-fed). 49 days later the animal died. Its blood was frequently examined up to the time of death, but never showed trypanosomes. Death in this case was probably due to a long captivity. Monkey 382, a duplicate experiment to 381, has never shown trypanosomes. Monkey 395 was injected with the contents of 10 flies which had fed 24 hours previously. It died 21 days later, never having shown trypanosomes. Monkey 396 was inoculated with the contents of ten "24-hour" flies. This animal was also uninfected. The natural conclusion is, that infection cannot be produced by inoculation of trypanosomes from the intestine of the fly, and this same conclusion was arrived at by Colonel Bruce when experimenting with the trypanosome of Nagana.

5. *Can trypanosomes travel from the intestine to the salivary gland of the fly?*

1. The salivary gland of a fly which had been infected 144 hours previously (and re-fed as usual) was dissected out. This fly contained great numbers of trypanosomes in its intestine, many of them showed forms with an anteriorly placed micronucleus. The salivary gland, on examination, showed numbers of actively motile trypanosomes. On staining, most of these trypanosomes appeared to be the ordinary forms as seen in the blood, but there were a few forms similar to those seen in the gut.

2. In the "fresh" fly noted above, which contained numerous trypanosomes of almost the ordinary form in its gut, the salivary gland was also found to contain numbers of trypanosomes. The salivary gland was broken up in normal salt solution and injected into a monkey, but it had been kept for some time before this was done, and the trypanosomes had lost most of their activity. In a stained preparation these trypanosomes were like the forms ordinarily seen in the blood of man or injected animals. Up to the present, 15 days, this monkey has not shown trypanosomes. None of the series of monkeys on which the flies were re-fed has as yet shown trypanosomes.

LONDON :

HARRISON AND SONS, PRINTERS IN ORDINARY TO HIS MAJESTY,
ST. MARTIN'S LANE.

REPORTS
OF THE
SLEEPING SICKNESS COMMISSION
OF THE
ROYAL SOCIETY

No. VII.

15. Histological Observations on Sleeping Sickness and other Trypanosome Infections.
By F. W. MOTT, M.D., F.R.S.

London
JOHN BALE, SONS & DANIELSSON, LTD.
OXFORD HOUSE
83-91, GREAT TITCHFIELD STREET, OXFORD STREET, W.

DECEMBER, 1906

Price 4/6 net.



HISTOLOGICAL OBSERVATIONS
ON
SLEEPING SICKNESS AND OTHER
TRYPANOSOME INFECTIONS

BY
F. W. MOTT, M.D., F.R.S.

(From the Pathological Laboratory of the London County Asylums)



London
JOHN BALE, SONS & DANIELSSON, LTD.
OXFORD HOUSE
83-91, GREAT TITCHFIELD STREET, OXFORD STREET, W.

—
DECEMBER, 1906

HISTOLOGICAL OBSERVATIONS ON SLEEPING SICKNESS AND OTHER TRYPANOSOME INFECTIONS.

By F. W. MOTT, M.D., F.R.S.

(From the Pathological Laboratory of the London County Asylums.)

(PLATES I—XI.)

It is now generally accepted that Sleeping Sickness is a chronic disease caused by the *Trypanosoma Gambiense*, the usual mode of infection being by a biting fly, the *Glossina palpalis*.

MATERIAL USED.

By the desire of the Committee of the Royal Society on Tropical Diseases, Colonel Bruce gave instructions to his assistants, and they have forwarded to me from Entebbe material from :—

- (1) Twenty-four cases of sleeping sickness in natives.
- (2) Portions of the brains of eight monkeys experimentally inoculated with *T. Gambiense*.
- (3) Two oxen infected with Jinga trypanosome (probably a species of *Nagana*), and one donkey infected with mule trypanosome.
- (4) The tissues of a monkey that died two years after infection by *T. Gambiense*, which showed the typical lesions of sleeping sickness recorded by Captain Harvey and Major Leishman.
- (5) The brain of a rabbit that died three months after inoculation with Surra.
- (6) The tissues of two European cases of sleeping sickness. The results of one case under the care of Sir Patrick Manson have been recorded. The histological examination of the other case, for the material of which I am indebted to Dr. Rose Bradford, will be published in full later, although it may be remarked that the results entirely confirm previous observations.

The tissues have been preserved in Formol or Formol-Müller solution, or they have been sent already embedded in paraffin after having been hardened for a short time in 5 per cent. formalin solution. Sections were cut of either 5 or 10 μ thickness.

STAINING METHODS.

The following staining reagents were used for the sections cut in paraffin :

(1) Romanowsky, Leishman, Polychrome blue and eosin. These stains were relied on to show the existence of trypanosomes or their degenerated products, lymphocytes, plasma cells and other cells in the meningeal and perivascular infiltrations. It was found that the polychrome blue and eosin also revealed the glia cells because the body of the cell and processes stain pink, the nucleus blue. These staining methods served also in conjunction with the Gram method for the discovery of micro-organisms.

(2) Heidenhain hæmatoxylin, Van Giesson and modified Mallory and Weigert methods were used for differentiating the neuroglia cells and their processes.

(3) The Marchi and New Weigert methods for showing the acute and chronic nerve fibre destruction. For this purpose the material was embedded in celloidin.

By one or several of these methods combined, observations were made regarding the following points :

(a) The existence of trypanosomes, degenerated products of trypanosomes or Leishman bodies.

(b) Changes in the nerve cells of the brain, spinal cord and spinal gangli.

(c) Changes in the pia-arachnoid membranes, the blood vessels and lymphatic structures especially with reference to (1) the endothelial cells, (2) the neuroglia cells, the branches of some of which form the supporting trabeculæ of the perivascular lymph spaces, and (3) the lymphocyte and plasma cell infiltration characteristic of sleeping sickness.

(d) The existence of micro-organisms.

(e) The degeneration of nerve fibres and glia substitution.

It may be mentioned that in a number of instances sections of the lymphatic glands, some of which were removed during life and others *post-mortem*, were examined by the same method. The principal pathological conditions observed were either drawn or photographed.

An epitome of most of the cases is given in the form of an Appendix to this communication, together with reference to notes and observations made at Entebbe by the members of the Commission under whose care the cases were. Also observations and notes made by myself on the examination of the tissues.

PART I.

INTRODUCTION.

IN every case of sleeping sickness in which symptoms of the disease were observed during life, I have found the same chronic meningo-encephalitis which I first described in 1898, and which has been since confirmed by the Portuguese Commission, and others. I did not in those two cases find evidence to support the view that this disease was caused by microbial infection, but in the material received since from Uganda, I was surprised at the large proportion of cases, nearly 80 per cent., which showed diplo-coccal or diplo-streptococcal infection. It is therefore not to be wondered at that the Portuguese authorities should at first have considered this organism the essential cause, or that Castellani should, before he discovered the trypanosoma in the cerebro-spinal fluid, have considered the diplo-streptococcus a specific micro-organism for this disease; or that he should have regarded it afterwards as playing an important part in producing secondary or terminal infection and causing the death of the patient, —with which I was myself in agreement. But numbers of facts have accumulated, conclusively establishing the etiology of the disease, (1) the death of Europeans suffering with *T. Gambiense* infection long after they have left the country where the disease is endemic; (2) the production of the characteristic lesions in monkeys by experimental inoculation; (3) the absence of the lesion in any other conditions of infection than trypanosome infection; (4) the chronicity of the disease as shown by European cases; (5) the existence of cases of sleeping sickness only when the *T. Gambiense* and the *G. palpalis* co-exist, as first demonstrated by Colonel Bruce. There is therefore no doubt that the trypanosome infection is *alone* the cause of the disease; but how the trypanosomes produce this characteristic, we might say specific, morbid change in the central nervous system we do not know. Nor has either histological examination or experiment so far solved the question.

There is a parallelism between the intensity of the lethargy, the chronicity of the disease, and the characteristic histological changes in the central nervous system.

Personal observations during life on cases which died in England, and reference to the symptoms and their duration, of cases at Uganda, convince me that the above statement is true, for I have found by microscopical examination of the tissues that those cases which showed the most pronounced cell infiltration of the membranes and the perivascular spaces were the most chronic, and exhibited during life most severe lethargy, *vide* cases 619 and 21. Whereas one case, which had long suffered with *T. Gambiense* in the blood and enlarged glands, but which manifested no signs of lethargy (*viz.*, Bara Risgallah, p. 31), died after a ten days' illness from pneumonia and pneumococcic meningitis, the brain and cord showing no perivascular cell infiltration in those situations where, in sleeping sickness, it is most abundant, namely, the subcortical white matter and the internal capsule.

The tissues of Dr. Bradford's case of sleeping sickness in a European who had left Africa ~~five~~^{three} years, and had therefore certainly suffered with trypanosome infection for that period of time, showed much more chronic and extensive histological change than the nervous tissues of Sir Patrick Manson's patient, who died of sleeping sickness in less than ~~three~~^{two} years after leaving Africa. My observations, however, serve to show that secondary microbial invasion of the blood was the immediate cause of death in the latter case not long after she had commenced to manifest signs of sleeping sickness (*vide* Bibliography).

MORBID CHANGES IN LYMPHATIC STRUCTURES.

The disease is characterised by a chronic polyadenitis (Greig), which is subsequently followed by a chronic inflammatory change in the lymphatics of the brain and spinal cord.

All the observers from the earliest time have noticed the enlargement of the lymphatic glands; and Greig, at my suggestion, punctured the glands and examined the fresh juice. He is of opinion, from his observations, that this is an easier and more reliable mode of determining the existence of *T. Gambiense* than examination of the blood or cerebro-spinal fluid. Dutton and Todd came to the same conclusion working in the Congo State. Many natives in Uganda and the Congo State have, however, enlarged glands, and yet are not the subjects of sleeping sickness. They may be, however, and probably in nearly all cases are, candidates for the disease.

Do the trypanosomes get into the glands and *multiply there*, setting up a chronic inflammatory process which terminates in fibrosis? The glands may be inflamed and enlarged, and yet be sterile as regards micro-organisms. It is probable that the trypanosomes infect the lymphatic glands by escaping from ruptured capillaries, or they may become infected by the cerebro-spinal fluid when this secretion contains trypanosomes. Similarly by capillary hæmorrhage the trypanosomes may infect the cerebro-spinal fluid and the lymphatic structures of the central nervous system. If the trypanosomes can set up chronic inflammatory changes in the lymphatic glands, (as there is no doubt they do), and microscopic examination of sections reveals but occasional and scanty evidence of their presence, it is quite reasonable to suppose that they can similarly produce chronic inflammatory changes in the lymphatic structures of the central nervous system. We do not know if the trypanosomes produce this chronic irritation by their mere mechanical presence, which seems unlikely, seeing that the vessels may be crammed with trypanosomes in Nagana and Surra, without causing lymphangitis. There is, according to Plimmer, Thomas and Anton Breine, however, no experimental evidence that trypanosomes produce a chemical toxin; although that would seem the most probable cause of the chronic inflammatory change. The numbers of trypanosomes found in the cerebro-spinal fluid are in no way proportional to the changes found in the central nervous system. Yet there is considerable evidence (*vide* Sleeping Sickness Reports, Royal Society), to show that not until trypanosomes are found in the cerebro-spinal fluid does the chronic inflammatory change take place. If they existed in abundance instead of sparsely, we might consider that this fluid afforded a suitable medium for their propagation, and the absence normally of leucocytes in this fluid might be accounted a cause. On the other hand, the small quantity of proteids which the cerebro-spinal fluid contains would not admit of suitable nutrition.

The posterior spinal ganglia always show some chronic changes, proliferation of the endothelium of the lymphatic capsules of the ganglion cells, together with interstitial lymphocyte accumulation; and these chronic changes may be due to the absorption of toxins from the neighbouring infected paravertebral glands.

In practically all cases of sleeping sickness, the cervical glands are enlarged, and the most chronic change is found about the base of the brain. Hence a probability that the chronic inflammation of the

lymphatics spreads along the nerves, spinal ganglia and roots to the central nervous system, and especially along the lymphatics of the nerves and vessels entering the base of the skull. Examination of other tissues, *e.g.*, the heart, pericardium, liver, alimentary canal and testicles, shows, though, generally speaking, in far less degree, an infiltration and accumulation of lymphocytes in the lymphatics, suggesting a defensive reaction. In fact, it might be considered that there is for a long period of time a struggle between the phagocytes and the trypanosomes in the blood, and it is not until the former commence to succumb in the defensive struggle of the organism, that the symptoms of sleeping sickness become pronounced. Certainly in very chronic cases I have been struck by the few polynuclears to be seen in the transected blood vessels as compared with small and¹ large-celled mononuclears, even when the patient has died with terminal microbial invasion.

The chronic inflammatory change of the nervous system is manifested by a proliferation and overgrowth of the neuroglia cells, especially of those which are related to the subarachnoid space and perivascular lymph spaces, with accumulation and probably proliferation of lymphocytes in the mesh work. In chronic cases plasma cells of Marscholko, similar to those in the lymphatic glands, may be found. Various other cells are met with in less numbers, some being the result of degenerative changes and others of endothelial origin, and possessing a phagocytic activity. The characteristic morbid change affects the soft membranes and the vessels.

The membranes.—By the several differential staining methods employed, sections of the cerebral cortex, the base of the brain, the cerebellum and the spinal cord exhibit a chronic leptomeningitis. The chronic inflammatory process is most marked where the cerebrospinal fluid is most abundant, and it consists of cell proliferation and cell infiltration.

The neuroglia.—There is a marked subpial felting in the molecular layer of the cortex in chronic cases; and in all cases there is some degree of subpial and septal proliferation of the neuroglia. It is not merely an increase numerically of the neuroglia cells, but an increase in size of the body of the cell, and increase in the number and thickness of the processes. In chronic cases it may be almost

¹ These large-celled mononuclears are the result of proliferative activity in the red marrow of bone. This tissue was not sent to me, but I have had the opportunity of examining bone marrow from one or two cases.

as pronounced as in some cases of general paralysis (*vide* figs., Plates II and III, and figs. 3 and 5, Plate IX).

Cell infiltration.—The irritative process affecting the arachnoid serous membrane is manifested not only by proliferation of the neuroglia cells contained in the adjacent nervous substance, but also by a proliferation of the endothelial cell-nuclei and an infiltration of the pia arachnoid membrane with lymphocytes which may become transformed into plasma cells of Marscholko. All stages of transition from a lymphocyte to a plasma cell can be seen just as in the inflamed lymphatic glands (*vide* fig. 4, Plate IV, and fig. 2, Plate I). These plasma cells, which are found more often in the perivascular infiltrations, have a characteristic appearance and staining reaction. As the cytoplasm of the lymphocyte grows the nucleus with its wheel-like chromatin particles remain at one end of the cell, and a clear halo separates one side of the nucleus from the cytoplasm. The nucleus stains blue, the cytoplasm pink (*vide* fig. 4, Plate IV).

The vessels.—The striking feature of this disease, distinguishing it from all other chronic nervous affections with which I am familiar, is the universal perivascular cell-infiltration of the central nervous system (*vide* fig. 3, Plate II). This infiltration is most marked and appears earliest in regions where the cerebro-spinal fluid is most abundant. It is therefore very marked about the vessels of the medulla and pons, the cerebellum and the arteries which perforate the base of the brain. It exists around the vessels of the whole of the pia corticalis and spinalis and is obviously related to the lymphatic system (*vide* plates and photomicrographs). As a rule I think the infiltration is more pronounced in the deep sub-cortical white matter than elsewhere. This may be due to the fact that the vessels of the deep sub-cortical white matter have a different source and distribution, and their surrounding lymphatics drain into the subarachnoid space at the base of the brain. An examination of any vessel in a well advanced case reveals characteristic appearances (*vide* figs., Plates I, II, and III). The infiltration under a high power is seen to consist of an extensive proliferation and increase in size of the neuroglia cells, which by their branching processes form the sustentacular framework (*vide* figs., Plate I, and figs. 1, 2, 3, 4, Plate II). Entangled in the mesh work are the lymphocytes and proliferated nuclei of the glia cells or endothelial nuclei.

The relative proportion of lymphocytes to the neuroglial and endothelial nuclei varies in different cases. There are other cells, viz.,

plasma cells of Marscholko (*vide* fig. 3, Plate I), also large round or oval cells with the nucleus staining deep blue and pushed up to one end or pole, the cytoplasm consisting of a number of clear spherules stained by eosin, giving the cell a mulberry appearance; hence I have called these cells morular cells. They correspond to the Körnchenzellen of Alzheimer. The appearance of these cells suggests degenerated plasma cells. Similar cells are seen in the degenerated structures of infected lymphatic glands. Besides these granulation cells, the result of degenerative processes, there are large macrophages containing red blood corpuscles in various stages of dissolution (*vide* fig. 5, Plate III). These macrophages containing blood corpuscles, when found in the subarachnoid space, indicate hæmorrhage into the cerebrospinal fluid, and suggest that this is the mode in which this fluid becomes infected by the trypanosomes.

Some degree of perivascular neuroglia proliferation was found in two cases of experimental sleeping sickness, when there was no obvious lymphocyte infiltration around the vessels. I have observed neuroglia proliferation in all cases of human sleeping sickness. The more chronic the case the more marked, as a rule, is the neuroglia proliferation; moreover, not only are the neuroglia cells more numerous but they are larger, and with more branching processes (*vide* fig. 1, Plate II). In the monkey, which showed the typical lymphangitis of the central nervous system characteristic of human sleeping sickness, the neuroglia proliferation was more marked than the lymphocyte infiltration. I have had the opportunity of examining the tissues of two European cases; one, which survived five years after leaving Africa, in which sleeping sickness symptoms were observed for more than twelve months; and the other, Mrs. S., who only survived ~~three~~² years after leaving Africa, and in whom sleeping sickness symptoms only existed a few months, death being brought about by diplococcal infection. Comparative observations showed that the former case exhibited much more advanced morbid changes in the lymphatics of the nervous system.

Whence come the lymphocytes in the perivascular spaces? We know that in chronic cases both the small and large mononuclears increase in the blood and the polymorphonuclears diminish; indeed, in some of the very chronic cases transections of the vessels showed hardly any polymorphonuclears, even though there had been a terminal diplo-streptococcal infection. Sometimes quite a number of small and large mononuclears can be seen amidst the red blood

corpuscles of transected vessels (*vide* fig. 1, Plate I). There is a considerable difference of opinion whether lymphocytes can migrate by diapedesis; according to Schultze and Ehrlich they are incapable of exhibiting amœboid movements. Ranvier, however, has observed amœboid movements in the lymphocytes squeezed from lymphatic glands, and Jolly has observed amœboid movements in lymphocytes taken from the thoracic duct.

It is very difficult to assert that the lymphocytes seen in the blood of vessels in sections do pass through the walls of the vessels. Certainly the appearances suggest that this may be the source of the lymphocytes in the cerebro-spinal fluid in sleeping sickness and other chronic diseases of the nervous system. There is, however, no proof that they do. What other hypothesis can be offered for this vast accumulation of lymphocytes in the perivascular lymph channels and spaces? The arachnoid space may be considered to be a serous sac, and there is a very close similarity in the appearances presented by the perivascular lymphatics of the nervous system in sleeping sickness, and the perilymphangeal nodules of developing lymphoid nodules of the omentum described by Klein, and figured in Quain's "Anatomy." The serous membranes and lymphatic channels and clefts of other organs may be affected in this disease, as shown by accumulations of lymphocytes (*vide* figs. 2 and 3, Plate X).

The meningeal and perivascular cell proliferation and infiltration of the central nervous system may be regarded as the result of a chronic irritative process connected with the presence of the trypanosomes in the cerebro-spinal fluid.

This cell proliferation and infiltration is made up of proliferated branching neuroglia cells, in which are entangled lymphocytes and proliferated endothelial nuclei and possibly young neuroglia cells with a small amount of cytoplasm. The origin of the lymphocyte infiltration is uncertain; it may be (1) that the lymphocytes come from the blood by diapedesis or by rupture of vessels, and having entered the cerebro-spinal fluid proliferation takes place; (2) that they accumulate in the obstructed lymph channels of the perivascular lymphatics; they may be formed by the proliferating nuclei of the lymphatic endothelial cells, the same as they appear to be in lymphatic glands. But besides, there is the chronic inflammation of the lymphatic glands, generally terminating in fibrosis, which may obstruct the drainage of the cerebro-spinal fluid from the closed cerebro-spinal cavity along the lymphatics of the cranial and spinal nerves. Universal chronic

inflammation of the lymphatic glands terminating in an obstructive fibrosis would tend to block the flow of the cerebro-spinal fluid and lead to accumulation of proliferating lymphocytes.

There is considerable difficulty in distinguishing between nuclei of glia cells and lymphocytes. The chromatin particles of the glia cells, usually two or three, lie in a pale nucleoplasm. The nuclei of the neuroglia cells are, as a rule, larger than lymphocytes (*vide* fig. 4, Plate II, and fig. 4, Plate X). They undergo active proliferation not only in the perivascular spaces but in the tissues. The young glia cells lie in pairs, or fours, or more, and may have but little cytoplasm surrounding the nucleus.

Examination of slides of the fresh juice of the glands obtained during life by puncture and stained for trypanosomes, proves conclusively that the cause of the glandular enlargement and of the chronic inflammatory changes met with, is the presence of trypanosomes. Yet the microscopic evidence of the existence of trypanosomes in the sections of the glands is not more satisfactory than the evidence of their existence in the perivascular and meningeal infiltration of the nervous tissue. Chromatin particles which may be micronuclei and macronuclei can be seen as well in one as in the other, and smears of fresh brain sometimes reveal trypanosomes just as the smears of glands.

Smears of glands removed during life from the necks of natives suffering with *T. Gambiense*, but not yet manifesting signs of sleeping sickness, *although sterile as regards micro-organisms*, showed trypanosomes and degenerated products of trypanosomes in the form of small and large chromatin rings (macronuclei and micronuclei). Sections of the same glands exhibited macronuclei and micronuclei and, occasionally, a trypanosome. As the glands were sterile, it may be presumed that the trypanosomes were the cause of the swelling and chronic inflammatory changes. The sections showed increased vascularity and lymphocytes in all stages up to the formation of large plasma cells of Marscholko (as shown in fig. 4, Plate IV.), and large numbers of degenerated swollen plasma cells like those seen occasionally in the perivascular lymph spaces of the brain in sleeping sickness. Moreover, some of the large cells appeared to be endothelial cells which have taken on a phagocytic function and eaten up lymphocytes and chromatin particles. The endothelial cells have proliferated in these inflamed glands, and there is a tendency to fibrosis, nuclear proliferation and thickening of the trabeculæ and walls of the lymph sinuses and vessels. Later these glands, when

the inflammation subsides, become fibrous, dense and less vascular. Quite similar appearances were observed in glands removed during life from the neck in cases of pronounced sleeping sickness. These glands were frequently sterile, but the majority which I received that were removed *post mortem*, and quite a number even removed during life, showed points of suppuration in their interior, and an infection with diplostreptococci. I have, however, come to the conclusion that these organisms only play the part of a terminal or late secondary infection due to the breaking down of the defences of the organism. This diplostreptococcal invasion must, however, play an important part in hastening the fatal termination.

In a discussion which took place at the meeting of the British Medical Association at Toronto, August, 1906, when I demonstrated the histological changes in the nervous system of some chronic trypanosome infections, Professor Welch called attention to the fact that Councilman had shown that in every fatal case of small-pox streptococcal invasion occurred. He asked whether the absorption of microbial toxins could be absolutely excluded as a cause of the histological changes. In reply I stated that, undoubtedly, the fatal termination was hastened in a large number of cases by the microbial invasion, and my observations had shown that a systematic examination of the lymphatic glands had led to the demonstration of organisms where microbial invasion had not been suspected. Yet the etiology of the disease and the study of some of the chronic fatal cases, and particularly the European case under the care of Dr. Bradford, showed that the trypanosomes, apart from microbial invasion, caused the characteristic changes in the nervous system.

In marked chronic cases of sleeping sickness the appearances presented by the lymphatic glands resemble in many ways the infiltration of the perivascular lymphatics of the central nervous system. In the latter there are proliferated lymphocytes, granule cells, plasma cells, proliferating endothelial cells, occasional degenerated trypanosomes and numerous chromatin particles, many of which are probably micronuclei and macronuclei, entangled in the markedly proliferated neuroglial sustentacular framework. Figs. 4 and 5, Plate V., show this correspondence of the histological appearance in the lymph sinus of the gland and the perivascular lymphatics of the brain.

We may therefore conclude that the presence of the trypanosomes in these perivascular lymphatics in the subarachnoid space (as evidenced by their constant existence in the cerebro-spinal fluid,

sometimes in such numbers as to be found without centrifuging) might cause, as in the lymphatic glands, this chronic lymphatic inflammation of the central nervous structures. Infection of the cerebro-spinal fluid may be from the lymphatic glands, or more likely from the blood by capillary hæmorrhages. The European cases and the few animals which have shown the characteristic lesions have all lived over eighteen months after infection; it consequently takes time to effect the change. Lymphatic gland-enlargement is characteristic of all forms of chronic trypanosomiasis of animals.

All cases of sleeping sickness have trypanosomes in the cerebro-spinal fluid at some time or other, and it is probable that the entrance of the trypanosomes into this fluid marks the onset of, and slowly causes, the chronic inflammatory change in the lymphatic system of the central nervous system. The alternative hypothesis is that the trypanosomes, by multiplying in the lymphatic glands, produce a toxin which is absorbed by the lymphatics, and this toxin proceeds along the vessels and nerves to the lymphatics of the cerebro-spinal axis, the route being especially from the cervical glands by the lymphatics of the large vessels and nerves entering the base of the skull.

This chronic inflammation of the lymphatics of the brain with perivascular glia cell proliferation, lymphocyte and plasma cell accumulation gradually and progressively interferes with the flow of the lymph stream and the circulation of the cerebro-spinal fluid. It is not decided whether the cerebro-spinal fluid functions as the lymph of the brain, or whether it simply forms a water jacket around the lymphatic sheath which is closely applied to the wall of the blood-vessel. The lymphocytes and glia cells certainly fill up this space and interfere with the normal outflow of the fluid from the cerebro-spinal cavity; consequently when lumbar puncture is performed there is usually evidence of increased pressure; moreover the fluid contains abundance of lymphocytes. This increased intracranial pressure interferes also with the circulation of the blood in the small vessels, and the characteristic symptoms of the disease, viz., lethargy, tremors and muscular weakness, may be explained by the functional depression of the nerve cells from a deficient nutrition and interference with oxidation processes, brought about by mechanical and bio-chemical interferences with the activities of the nerve cells, and not by neural destruction. This is shown by the patients retaining comprehension of their surroundings and by their intelligent response to questions when roused from their

lethargy. A totally different picture to general paralysis (also a meningo-encephalitis) in which there is a profound parenchymatous change, whereas sleeping sickness is a *primary interstitial process*; although later on in the disease, especially when it is chronic and of long standing, marked chromolytic cell changes and a certain amount of destructive degeneration of the neurons do occur.

CHANGES IN THE SMALL VESSELS AND CAPILLARIES.

The capillaries in the pia and in the brain tissue show the following changes, but these are not nearly so marked as in general paralysis of the insane.

The nuclei of the endothelial cells may undergo proliferation, and in the neighbourhood of the capillaries and small vessels there are often numerous lymphocytes, plasma cells and glia cells; but I fail to find evidence of sprouting new capillaries as seen in general paralysis, nor can I but very rarely find any evidence of the Stäbchenzellen or rod cells described by Alzheimer, and regarded by him as very characteristic of this disease. These Stäbchenzellen, I consider, are probably collapsed capillaries (*vide* fig. 6, Plate II).

Capillary hæmorrhages are met with in all forms of trypanosome disease, and probably are the result of obstruction by the organisms.

CHANGES IN THE NEURAL ELEMENTS.

Although the meninges are in many cases obviously thickened and the convolutions flattened (indication of some intracranial pressure), yet there is no naked eye wasting of the brain. The depth of the grey matter of the cerebral cortex is not appreciably diminished, although the vessels both in the grey and white matter may appear somewhat congested. In very chronic cases, after the brain has been hardened in formol-Müller solution, then washed in water, the transections of the vessels may appear like dark dots surrounded with a pearly grey ring. The dark centre is due to the blood contained in the vessel, and the surrounding zone of a pearly grey colour is due to the perivascular cell infiltration.

I have not observed granulation of the ependyma of the ventricles, so characteristic of the meningo-encephalitis of general paralysis of the insane. Moreover the wasting of the grey matter of the cerebral

cortex, so characteristic of this disease, is not met with in sleeping sickness. The convolutions are broad and of normal size, and the sulci tend to be obliterated in sleeping sickness; whereas in general paralysis the convolutions are shrunken from atrophy of the neural elements, cells and fibres, and the sulci are consequently broad and deep. In both diseases there is obvious meningeal thickening, and septal and perivascular changes, but here it seems to me the similarity ends. But this statement becomes more apparent and convincing when the microscopic changes are described. Moreover, a comparison of the size of the remaining structures of the central nervous system show that in general paralysis there is a primary neuronie atrophy which does not occur in sleeping sickness. Thus to the naked eye the spinal cord in the latter disease may appear normal as regards amount of grey and white matter, whereas in general paralysis the cord is often much reduced in size, and there is very obvious neuronie atrophy.

The naked eye appearances therefore point especially to a primary parenchymatous degeneration in general paralysis with chronic interstitial and meningeal inflammation, whereas in sleeping sickness the morbid change is primarily interstitial and with some secondary parenchymatous atrophy.

MICROSCOPIC EXAMINATION OF THE NERVE CELLS AND FIBRES.

Cells.—Stained by the various modifications of Nissl method, sections of the various structures of the central nervous system, viz., cortex cerebri, cerebellum, pons, medulla oblongata and medulla spinalis, also spinal ganglia, exhibited certain changes, but in comparison to the interstitial perivascular and meningeal change they were inconsiderable, thus contrasting markedly with general paralysis.

Let us consider, firstly, the cortex cerebri. Under a low power, the five layers of Meynert can usually be easily differentiated. The most obvious change is in the subpial molecular layer of Cajal, but the three layers of pyramids above the layer of granules are usually distinctly seen, the cells usually retaining their pyramidal form, their apical processes being straight as a rule, and the cells arranged in columns, a picture quite different to that seen in general paralysis.

The abnormal feature, apart from the perivascular infiltration, is the abundance of nuclei of neuroglial cells and lymphocytes scattered about and often lying in groups in the perineuronal spaces (*vide photomicro*).

The great majority of the specimens of nervous tissues from sleeping sickness cases which I have examined, have shown marked changes in the ganglion cells of the central nervous system when examined under a high power. I have reason to believe that these changes are largely due to the effects of secondary or terminal microbial infection, to pyrexia, or in some cases, hyperpyrexia. But a terminal or secondary microbial invasion with toxæmia and fever would produce universal effects, and in such cases one finds that throughout the nervous system the ganglion cells present a chromolytic change, the whole ganglion cell staining with polychrome and eosin a diffuse purple, and showing an absence of the Nissl pattern of the cytoplasm. In the first case I examined in 1898, the patient died of septic hyperpyrexia from an abscess in the lung. Although the interstitial meningeal and perivascular change was most pronounced, the neuronc degeneration was comparatively slight, although the patient was in the third stage of the disease. The outline and shape of the ganglion cells of the central nervous system did not present marked changes, but every cell showed a diffuse chromolytic change. This was obviously due to the high fever. Nevertheless, in chronic cases marked chromolytic changes and atrophy of dendrons do occur in the ganglion cells, especially in those regions where the perivascular infiltration is most severe, and where, in consequence, a certain amount of blood stasis takes place. I have observed this in the medulla oblongata; and the affection of the important cardiac and respiratory centres in this region may, in a few uncomplicated cases, be the ultimate cause of death. The changes in the ganglion cells may therefore be considered as due (1) to the primary lymphangitis, and (2) to secondary microbial toxæmia. It is difficult to differentiate the cells which are affected by the one cause from the other.

I consider, however, that the chronic change is indicated in those cells in which (1) there are appearances of atrophy of the dendrons, the protoplasmic processes being either attenuated or broken off; (2) the cytoplasm still exhibits some remnants of a pattern of Nissl granules in the circumference of the cell and on the dendrons; (3) the nucleus is large and clear and often eccentric. Sometimes a dead ganglion cell may be seen being devoured by phagocytes (*vide* figs., Plate VI). The cells of the spinal cord usually show much less change than the cells of the medulla oblongata and cerebral cortex. The cells of the posterior spinal ganglion usually show chromatolysis, but not destruction (*vide* fig. 1, Plate VII).

The appearance of the cells in acutely fatal trypanosome infections, *e.g.*, Surra and Jinga in animals, could be accounted for by the anæmia caused by the blood change and the obstruction of the small vessels by the trypanosomes. In the brain of the rabbit dying of Surra, the ganglion cells all showed a shrinking of the cytoplasm, a marked chromatolysis and disappearance of the Nissl granules, and swelling of the nucleus, and a change not unlike that observed in some forms of experimental anæmia (*vide* fig. 3, Plate VIII).

CHANGES IN THE CENTRAL CANAL OF THE SPINAL CORD.

Not only is there evidence of a chronic irritative action of the cerebro-spinal fluid by the cell proliferation in the meningeal and perivascular lymphatics, but in all chronic cases the central canal of the spinal cord is filled up owing to a proliferation of the cells of the ependyma. I found this had occurred in quite juvenile subjects. It was so in the little Congo negro boy, who died in Charing Cross Hospital in 1898, and I was of opinion then that this fact afforded evidence of a very chronic nervous affection caused by some irritating agent (*vide* fig. 1, Plate X). It was the same with the juvenile cases from Uganda, Sempagana, aged 8, Hamesi, aged 12, and Kaperi, aged 8-10. Such change denotes, then, a chronic process of considerable duration. It is probable in the light of our present knowledge of the possible long duration of the disease that these subjects were infected when quite infants.

Examined under a high power, the nuclei of the cells lining the spinal canal may often be seen undergoing active proliferation, and specimens stained with polychrome and eosin exhibit large pale nuclei with a thin membrane and chromatin granules stained blue surrounded by a pale pink amorphous substance. In the grey matter around the central canal numerous glia cells having a similar appearance can be seen.

EXAMINATION OF THE CENTRAL NERVOUS SYSTEM FOR FIBRES BY WEIGERT AND MARCHI METHODS.

In cases uncomplicated by terminal microbial infection there is a certain amount of fibre atrophy proportional to the cell atrophy described. This atrophy is most obvious in the tangential layer of the cortex cerebri, where the fibres in places are greatly diminished, or even absent. There may also be some diminution of the fibres in the super-radial and inter-radial systems, especially in chronic cases. There is, however, in the brain as in the spinal cord, no definite

system-tract sclerosis, the result of atrophy of a neuronie system (*vide* figs. 1, 2, 4, Plate IX). Generally in the lateral columns corresponding to the pyramidal systems some degenerated fibres can be seen by Marchi method, but the glia proliferation tends to follow the distribution of the septa rather than to accord with any definite atrophy of a system of nerve fibres (*vide* fig. 5, Plate IX).

By Marchi method, the cerebrum, cerebellum, spinal cord and spinal ganglia were examined in a number of cases. In most instances the results were unsatisfactory owing to a generally diffuse blackening of the myelin sheaths and the deposition of black granules. I consider this change¹ was probably the result of acute changes in the myelin, brought about by terminal microbial toxæmia, fever, &c. Some few of the cases, however, did not show this generalised change in the myelin, and a certain number of fibres showing Wallerian degeneration were found. These changes we may regard as definite and indicative of neuronie decay.

The results above described tend to show that a chronic trypanosome infection of the cerebro-spinal fluid causes a meningo-encephalitis and myelitis characterised by a chronic interstitial inflammation of the lymphatic structures of the central nervous system, and the cell proliferation induced thereby precedes and is far in excess of the parenchymatous change, contrasting markedly therefore with the meningo-encephalitis of general paralysis. It resembles general paralysis by the infiltration around the vessels of lymphocytes and plasma cells and by the neuroglia proliferation.

In sleeping sickness, even in advanced stages of the lethargy, the patient when aroused comprehends and responds in an intelligent manner to questions, proving that his associative memory is intact. Although he readily becomes fatigued and his speech and movements are tremulous, denoting impairment of highest motor innervation, yet there is no evidence of dementia as seen in general paralysis.

These clinical facts, which broadly separate these two diseases, entirely accord with the pathological changes. The neural elements in sleeping sickness are functionally impaired by the interstitial change, but when the patient is roused the neural elements of mind are still capable of functioning for a short time in a normal manner. But in general paralysis, where the interstitial change is less marked but the parenchymatous degeneration is progressive and destructive of neural elements, the mind is proportionally incapable of functioning normally.

¹ I have observed this in other diseases when there has been an infective process, especially when the tissues have been placed in formol-Müller. I do not, therefore, attach much importance to it.

In conclusion, it may be asked, If the trypanosomes are the cause of this chronic inflammation of the central nervous system, why are they not found in the infiltration and in the blood in sections?

The *T. Gambiense* is only found by careful search in blood films. They are seen with great difficulty in sections unless they exist in the blood in considerable numbers.

SECONDARY OR TERMINAL MICROBIAL INVASION.

After death, in the great majority of the cases which I have examined secondary or terminal microbial infection had occurred.

Sometimes the diplococci were found in sections of the blood vessels as well as in the membranes, indicating a generalised infection (*vide* fig. 2, Plate V., and fig. 6, Plate IV).

The culture experiments of Novy and McNeal show that infection of the culture media by micro-organisms interferes with the growth of the trypanosomes. The cases in which I found trypanosomes in the blood contained in sections of vessels of the nervous system, were two chronic cases uncomplicated as far as I know by microbial infection. In the European case, under the care of Sir Patrick Manson, the histological investigation of which Low and I reported, the trypanosomes disappeared from the blood a short time before death; this was coincident with a generalised diplo-streptococcal invasion.

How far diplo-streptococcal invasion of lymphatic glands may generate toxins without general blood infection and induce chronic changes in the lymphatics of the central nervous system I am not prepared to say.

The fact that swollen glands in the neck removed during life are sterile does not prove that other glands in the body, which cannot be removed are sterile. Deep seated glands may be infected by micro-organisms. Possibly it may be shown that as long as the body is able to resist bacterial invasion the trypanosomes are unable, by themselves, to produce the changes which cause sleeping sickness. There is, however, very little evidence of this hypothesis, and it must be assumed that in some way (which we have not at present discovered) the trypanosomes, or some modified form of them, set up this lymphangitis of the central nervous system. When there was an invasion of the central nervous system by diplococci, it seemed probable that this occurred by way of the lymphatics proceeding from infected paravertebral glands. Sections of the cervical nerves, spinal ganglia and posterior roots in some cases enabled me to trace the course of the microbial infection (*vide* fig. 1, Plate IV).

PART II.

Experimental Evidence.—Animals inoculated with *T. Gambiense* usually die before the characteristic lesions of the nervous system can occur. I have examined the tissues of nine animals (monkeys) which were inoculated at Entebbe in one way or another with *T. Gambiense*. They were all said to have exhibited the characteristic lethargy, but it is very difficult to differentiate (according to my experience) between a monkey that sits moping when profoundly ill, and an animal which exhibits a lethargy on account of the brain lesion.

The tissues of the brains of all the animals sent to me, with the exception of two, showed no characteristic change. The vessels of the brain were empty and there was no meningeal or perivascular infiltration. Several of these animals had survived the infection (as proved by the existence of trypanosomes in the blood) one year. One was subsequently infected with diplo-streptococcus from a sleeping sickness case; yet there was no sign of the meningo-encephalitis met with in every case of human sleeping sickness. This was the experience apparently of Ayres Kopke.

(1) The tissues of one monkey inoculated with *T. Gambiense* showed, however, the characteristic lesion of human sleeping sickness. This case was reported by Major Leishman and Captain Harvey. It survived the infection eighteen months. I have examined portions of the tissues kindly given to me by Major Leishman and find that there is a very marked neuroglia proliferation of the perivascular lymphatics, endothelial cell proliferation and lymphocyte accumulation, and a few plasma cells around the vessels of the brain in all the situations examined. In fact, the lesion in no respect differs essentially from that of human sleeping sickness (*vide* fig. 2, Plate III). The cerebro-spinal fluid and tissues in this case were, according to Leishman, sterile.

(2) A monkey, upon which large numbers of infected flies were allowed to feed on several successive occasions, exhibited trypano-

somes in the blood and cerebro-spinal fluid, and died eight months after the first fly feeding, having presented symptoms of lethargy. Reports of the Sleeping Sickness Commission of the Royal Society, No. VI., pp. 107 and 108.

The subcortical white matter of this animal showed a considerable glia cell proliferation in relation to the vessels (*vide* fig. 1, Plate III), but there was little evidence of lymphocyte accumulation. The spinal cord also showed a glia proliferation (*vide* fig. 3, Plate IX). It is possible, therefore, that the glia cell proliferation precedes the lymphocyte accumulation in the perivascular spaces.

(3) Monkey 99. The medulla oblongata and tissues about the base of the brain showed a commencing subpial, septal and perivascular glia proliferation.

Examination of the nervous tissues of animals inoculated with Nagana, Surra and Jinga trypanosomes, and which died within a few months of infection, the blood swarming with trypanosomes, or modified or degenerated trypanosomes, showed no perivascular or meningeal changes.

(1) The brain of a rabbit inoculated with Surra, which died three months later, was kindly given me by Dr. Plimmer, and showed the following appearances in sections. By any of the staining methods employed nearly all the blood-vessels showed masses of trypanosomes, as the coloured drawings exhibit (*vide* figs. 2, 3, and 4, Plate VIII). Single trypanosomes could be seen in the capillaries; in the larger vessels solitary trypanosomes and whorls of trypanosomes and plasmodial masses, which are either degenerated trypanosomes consisting of a zoogloæal mass in which many deeply-stained macro-nuclei and micro-nuclei can be seen, or of amœboid forms, described by Plimmer and Bradford. But in spite of this extraordinary trypanosome infection the blood-vessels showed little or no inflammatory reaction. The perivascular lymph spaces showed no lymphocytes; and the ganglion cells showed only marked chromolytic changes; otherwise there was nothing noteworthy in the nervous system.

(2) The brains of two oxen infected with Jinga trypanosomes were examined. The animals died within three months of infection; the results of the examinations were extremely interesting and will be given in some detail.

Experiment 162 (loc. cit., p. 171).—The cortex cerebri, the cerebellum, medulla and spinal cord were examined, and all yielded the same results. With a magnification of 1,200 diameters, the

capillaries and vessels were found to contain chromatin bodies closely resembling Leishman bodies, except that they were smaller, measuring from 1 to 2 μ , much more frequently 1 μ , rarely as large as 2 μ . They were either circular or oval rings, or had the appearance of the chromatin particles situated at the two poles. Several drawings from photomicrographs are given to illustrate their appearance and their numbers. Some of the capillaries show immense numbers, and in some transections of larger vessels these bodies may be observed lying in a zooglœal mass (*vide* figs. 3, 4; and 5, Plate VII).

Individual bodies exhibit some diversity in their form, indicating division. A large number of stained particles (which may be micro-nuclei) can be seen.

The Jinga trypanosome, as the accompanying drawing shows (*vide* fig. 2, Plate VII), is comparatively a large organism, as seen in the blood of a monkey, which was inoculated with it. Its oval macro-nucleus is much larger than these chromatin bodies which are seen in the vessels. If these chromatin bodies, as Leishman would affirm, are the macro-nuclei of trypanosomes, then it is difficult to explain why a dozen or more of the chromatin bodies can sometimes be seen lying in a space which could be covered by one trypanosome. Still, the trypanosomes may have degenerated elsewhere and the macro-nuclei have been carried into the capillaries. In view, however, of the researches of Captain Rogers regarding Leishman bodies being altered phases of trypanosomes, and the contention of Plimmer and Bradford *re* the existence of amœboid forms of trypanosomes, it is possible that these chromatin bodies may be some phases in the life of the trypanosomes in the blood. For comparison a drawing is given of the appearances presented by Leishman bodies in the spleen and splenic blood from preparations kindly lent by Sir Patrick Manson. The preparations were made from a fatal case of Kala-Azar.

Experiment 202 Ox (loc. cit. p. 174).—This animal died within three months of infection. Portions of the brain were stained in bulk by polychrome and eosin and sections cut 5 μ thickness after embedding in paraffin.

In this way the contents of the vessels were but little disturbed so that trypanosomes existing in the serous fluid contained in the blood vessels were recognisable in great numbers. The appearances of the trypanosomes and their modified forms are seen in fig. 1, Plate VIII.

It may be mentioned that in these two cases there was no sign of meningo-encephalitis, and there was no diplo-streptococcal infection. The ganglion cells showed chromolytic changes, and there were *many minute capillary hæmorrhages*, probably due to plugging of the capillaries by the organisms. I have frequently observed in the lymphatic glands, meninges and perivascular lymphatics of the brain of sleeping sickness, chromatin rings, very similar to, only smaller than the chromatin rings seen in the vessels of Jinga and Surra infected animals, of the trypanosomic origin of which there can be no shadow of doubt. It is therefore probable that a number of the chromatin particles seen in the tissues of sleeping sickness are all not *débris* of degenerated cells but *débris* of degenerated trypanosomes or their modifications. Especially would this argument be valid if the tissue, as in the case of the glands removed during life, had been shown to be sterile. Moreover, I have seen appearances in sections of lymphatic glands removed during life, of threadlike attenuated forms of trypanosomes resulting from division, not unlike those figured by Gray and Tulloch as multiplying by fission in the stomach of the *G. palpalis* (*vide* figs. 1 and 2, Plate V).

The experiments on animals, together with the examination of the central nervous system of a horse that died of dourine more than two and a half years after infection (a full account of which has been published in the **Proceedings of the Royal Society*, B., Vol. 78, 1906), tend to show that chronic trypanosomiasis is attended by a chronic lymphatic irritation. This irritation is manifested in the nervous system by a neuroglia proliferation, and subsequent lymphatic proliferation and accumulation.

Animals that die within a few months of inoculation have not survived a period of time long enough to manifest this neuroglia proliferation.

It is probable that animals infected directly by blood from sleeping sickness cases containing *T. Gambiense* might, if they were inoculated in the abdomen or hind legs, show changes in the spinal cord before they showed changes in the brain. This may account for the fact that Plimmer's rats only showed changes in the spinal cord; and in dourine or *mal de coit* the changes in the central nervous system are

* Since the above was published Dr. Lingard has kindly forwarded to me from the Imperial Bacteriological Laboratory of India the nervous tissues of other animals that have died of Dourine, wherein I have found the same change, though less marked.

primarily and most markedly severe in the lumbo-sacral region of the spinal cord, especially of the posterior and lateral columns.

Further experiments on animals should, in my opinion, be carried out, anthropoid apes being used, and the neck should be chosen as the seat of inoculation.

In conclusion, I have to thank my assistant, Mr. Chas. Geary, for valuable assistance in making the microscopic preparations, and Miss Agnes Kelley for assistance in making preparations, especially for the very accurate and beautiful drawings illustrating this Report.

I have appended a short report of the changes in the glia tissue of sleeping sickness by Dr. Georg Eisath (see next page).

ADDENDUM.

A DETAILED DESCRIPTION OF THE NEUROGLIA CHANGES IN THE BRAIN AND SPINAL CORD OF EIGHT CASES OF SLEEPING SICKNESS. BY DR. GEORG EISATH, Hall, Tyrol.

Dr. Eisath has for some time past been investigating the changes in the neuroglia by a special differential method of staining, which he has described in a communication entitled "Ueber normale un pathologische Histologie der Menschlichen Neuroglia." *Monatsschrift für Psychiatrie und Neurologie*. Band xx.

As he was working upon this subject in my laboratory, I placed at his disposal the nervous tissues of eight cases of human sleeping sickness which, by reason of their condition and mode of hardening and preservation, were suitable for staining by his method.

Subjoined is a translation of the account which he has kindly sent me of the results he obtained. They confirm and amplify the observations which I have described in this Report.

To Dr. Eisath is due the credit, by his differential method of staining, of showing the relative importance of the glia cell proliferation in the perivascular infiltrations and the quantitative relationship of glia nuclei to lymphocytes in this disease.

(1) *The character of the glia cells and their differentiation from lymphocytes.*—(a) The nuclei of the glia cells almost universally show a distinct nuclear membrane and possess normally two to three nuclear bodies, besides other small granules. The leucocyte nuclei are of many forms; some are round and possess an abundance of granules, others are lobulated and have an indistinct outline.

(b) The glia nucleus forms quite one-third of the transverse diameter of the cell, whilst the nucleus of the leucocyte fills up the greatest part of the cell. That is to say, the glia cell has a relatively much larger proportion of cell protoplasm than the leucocyte.

(c) The protoplasm of the glia cell is arranged in a star-like manner around the nucleus; and the border of the cell, in normal conditions, is very distinctly seen, whilst in the leucocytes it is not.

(2) *The distribution and localisation of the glia proliferation.*—The glia overgrowth is demonstrable in every case and the cells are

both increased in numbers and size. Giant glia cells were observed, and in every case the Weigert fibres are increased.

In the molecular layer of the cortex of many cases the glia cells are increased and often show an abundant formation of Weigert fibres, especially around the vessels. In the Meynert ganglion cell layers the increase of glia cells is relatively much less developed than in the superficial layer of the cortex, and in the white substance. The Weigert fibres, moreover, are only sparingly seen. In one case (Kirongo) the fibre formation is hardly demonstrable, and glia cells with surrounding protoplasm and processes are hardly recognisable in the cortex. The glia overgrowth in the white substance is, however specially observable around the larger vessels. *It exists not only around those vessels which show leucocytic infiltration, but also around capillaries where infiltration with round cells has not occurred.*

In the medulla oblongata the overgrowth and the morbid changes are most extensive.

In the spinal cord an extensive overgrowth of glia tissue exists by which the individual nerve fibres are surrounded, and this overgrowth affects all the tracts as well as the grey matter. There is no appreciable outfall of the medullated fibres, *only here and there and quite sparsely have the medullated fibres disappeared.* The glia cells are numerically increased and increased in size beyond the normal.

(3) *Pathological changes in the glia cells.*—The glia granular substance was not precisely investigated in this work and shows, so far as the researches extend, in the round glia cells *no marked pathological changes.*

Isolated glia cells possess well developed protoplasmic processes, others enormously increased Weigert fibres. Some of the glia cells have a uniform *homogeneous stained protoplasm* as if the nuclear substance had dissolved out or had disappeared.

Such cells usually have a dark brown stained nucleus, whilst others may have lost their processes and are converted into *hyaline balls.*

APPENDIX.

NOTES OF THE CASES OF SLEEPING SICKNESS AND ANIMALS EXPERIMENTALLY INOCULATED, WITH THE PRINCIPAL FACTS OBSERVED ON MICROSCOPIC EXAMINATION OF THE TISSUES.

- (a) Brief abstract of notes of clinical records.
- (b) Microscopical examination of tissues.
- (c) Remarks.

1. Nabujam, aged 30; died April 4, 1903. Sent as a case of sleeping sickness, turned out to be a case of tumour cerebri. No trypanosomes.

Microscopical Examination.—No meningo-encephalitis; no micro-organisms.

2. Zakibu. Admitted March 22, 1903.—Enlarged glands, tottering gait, temperature normal, no tremors. April 14.—General convulsions, left facial palsy. April 16.—Death. Trypanosomes in cerebro-spinal fluid; pneumonia—pneumococcal invasion of blood. Brain surface injected; Subarachnoid fluid excess—dull and opaque; no sign of active or acute meningitis. The substance of the brain appears healthy to the naked eye.

Microscopical Examination.—Chronic meningo-encephalitis; pneumococcic invasion; vessels of brain in places plugged with cocci.

3. Nonbi. Admitted February 23, 1903.—States that three brothers and four sisters all died of sleeping sickness. April 18.—General condition: Enlarged glands, no *trophic changes*. She is well nourished; pronounced nervous symptoms. She is conscious and tries to answer questions, but cannot. She lies all day absolutely torpid, with her eyes open. There is slight lateral nystagmus—pupils equal, no reaction to light; twitching of muscles, knee jerk absent, no ankle clonus. Died April 20.—Trypanosomes in cerebro-spinal fluid. *Post mortem.*—No signs of pneumonia; pericarditis. Brain: Dura mater normal; convolutions of the surface of the brain are flattened, the sulci filled with opaque-looking subarachnoid fluid; the vessels are injected, otherwise nothing abnormal.

This is an ordinary case of sleeping sickness. The anæmia may have been helped by ankylostomata. The pericarditis is an uncommon feature; meningo-encephalitis, peri-vascular infiltration very marked; great numbers of diplococci in the membranes—between the cells and in the leucocytes; well-marked advanced glia proliferation, especially of deeper layers of cortex and subjacent white matter. Microscopic examination indicates a chronic case.

4. Kaperi, aged 8 to 10 years.—Trypanosomes in the cerebro-spinal fluid. Case of purulent meningitis. Remarks: "In our experience these acute inflammatory cases are not usual. In this case it is evidently due to

streptococcal invasion. This appearance is not typical of sleeping sickness : as a rule, there are no signs of acute inflammation, but merely a flattening of the convolutions, an injection of vessels, and an excess of subarachnoid fluid " (p. 39, vol. i., Sleeping Sickness Reports).

Brain and spinal cord: No glands or other tissues sent; acute diplo-streptococcic meningitis, the whole of the meninges affected; mostly a polymorpho-nuclear exudation; not much extension to perivascular lymphatics of the nervous substance in the cortex and spinal cord, but fairly well marked in the medulla oblongata and base of brain (probably the primary seat of the infection by the micro-organisms). In the medulla oblongata there are vessels in which the inflammatory exudation shows numbers of mononuclear leucocytes, and amorphous red-stained granules of varying size from 1μ to 2μ or more—probably the result of coagulation necrosis of the broken-up chromatin particles of the polymorpho-nuclear leucocytes, and also the diplococci in their capsules. No trypanosomes seen in any of these sections. The ganglion cells show acute chromolytic and coagulative necrotic changes.

5. *Dr. Nabarro's Case.*—Some material was sent to me by Dr. Nabarro. The patient died of pneumonia. The ordinary meningo-encephalitis, characteristic of sleeping sickness, was found, and diplococci in the blood of transected vessels and in the inflammatory products.

6. *Dreya.* Case 69, E. E.—Admitted February 6, 1903; died June 12, 1903. A chronic case (*vide* fig. 1, Plate XI). Trypanosomes were obtained by lumbar puncture on June 2. Appearances of brain typical of sleeping sickness. Central nervous system examined: no lymphatic glands sent. All the appearances of a chronic meningo-encephalitis. Very marked perivascular infiltration of the whole central nervous system, especially of the base of the brain and medulla oblongata. No polymorpho-nuclears seen in the inflammatory exudation, which consists almost entirely of proliferated glia cells of mononuclears and plasma cells of Marscholko, also a number of morular cells. The exudation, as seen in the drawing, is most extensive, and extends to the smallest vessels, leading to their obliteration in some instances. The capillaries are seen often to contain yellow amorphous material instead of corpuscles. In the meningeal infiltration, also in the perivascular lymphatics are seen a great number of granule bodies of various sizes. It was thought that some of these granules might be the products of degenerated trypanosomes, as appearances like a macro-nucleus and micro-nucleus occasionally were seen. The great majority of the granules were, however, probably products of coagulation necrosis of nuclear chromatin particles of dead cells. The ganglion cells, especially of the medulla oblongata, were profoundly changed. The dendrites were broken off, the perikaryon pale, and either devoid of Nissl granules or were broken up; the nucleus was swollen, clear, pale, and often eccentric. The pigment was increased; all these changes pointed to a chronic degenerative change, which *may be* due to the action of the noxious agent which produces the inflammatory change, but more likely the result of nutritional defects occasioned by the vascular changes. Very occasionally a transected vessel would show a portion of a trypanosome, and one vessel showed, in addition, a whole organism.

7. *Case 248.*—Suleman Bin Mahomed, aged about 45 years, Persian, the first Asiatic to be affected at Entebbe. Came originally from Bushire on Persian Gulf. October 28.—History: Has been in Africa twenty years, of which he spent the first two years in East Africa. Has been in Uganda, on and off, for eighteen years, and has been down to the coast twice in that time. Latterly he has been a “headman” in the Government Transport Department, and when at Entebbe has lived near the lake. In fact, for some time he has lived almost like the natives and with them. He became ill two months ago, and was then seen by Dr. Hodges, whose report is as follows:—

September 2.—There are general tremors, anæmia, slight pyrexia (temperature 100° F.). Weak, irregular, rapid pulse. Spleen slightly enlarged. Left otitis media. Blood films examined, malaria found. October 28.—Lumbar puncture performed. Numerous trypanosomes seen in first field. Many lymphocytes. No red blood corpuscles.

October 31.—Present state. Patient is a very tall man, obviously wasted and ill. There is a heavy, sad look about the face and eyes, *vide* photograph. General condition very weak and feeble; gait weak and staggering. Voice weak. Marked tremor of tongue and lips. Slight tremor of fingers and hands. There is a fairly marked tremor of the body and head. No enlarged glands about neck, slight in groin (due to sore feet). Has pain in left ear, due to otitis media. Pulse fair tension, 68 per minute. Knee-jerks sluggish. Heart sounds feeble, no bruit.

November 6.—Photograph taken (*vide* fig. 2, Plate XI). November 12.—Patient has improved to a certain extent since he has been in hospital. Died later.

The brain showed the typical characters of sleeping sickness. No glands sent.

Microscopical Examination.—Chronic meningo-encephalitis fairly advanced. Not much change in form of the ganglion cells of the cortex; Meynert's columns fairly well seen, but obvious acute toxic change, as all the cells stain diffusely with the blue and erythrosin a dull purple—doubtless, an acute toxic change due to terminal microbial infection. Many of the transected vessels show plugs of streptococci—I have never seen so many in the blood in any condition previously; short bacilli are seen also in great abundance in the perivascular spaces (*vide* fig. 6, Plate III).

In the remaining cases the deep paravertebral glands of the neck, and often other lymphatic glands, were forwarded at my request, together with the adjacent nerves and posterior roots and ganglia, from a good few of the cases.

8. *Case 69, Q. Q.*—This was described as an acute case of sleeping sickness. No other notes.

Lymphatic glands: Paravertebral cervical glands filled with diplo-streptococci, and in places causing points of suppuration. Great plugs can be seen in the lymph channels, and no doubt the escape of these into the blood stream led to the general infection and death. Other parts of the gland show signs of chronic inflammation and necrosis; plasma cells are abundant, also granules of varying size. No definite trypanosomes seen. Posterior spinal ganglion with commencement of cerebro-spinal nerve

and spinal roots from cervical enlargement near the glands above described. There is a very marked perivascular infiltration; the capsules of the cells are also crammed with lymphocytes and the small vessels hardly observable normally in the roots and the mixed cerebro-spinal nerves are now readily discernible by the abundance of mono-nuclear cells accumulated in their lymphatic sheaths. The loose vascular connective tissue around the ganglion is also crowded with lymphocytes. Diplococci and streptococci with capsules are seen everywhere along the course of the lymphatics; in some places they form a regular injection (*vide* fig. 1, Plate IV).

Central nervous system: There is a generalised meningo-encephalitis throughout, more marked in the cerebellum and around the perforating vessels of the basal ganglia and internal capsule than elsewhere. Many small vessels are seen plugged with organisms (*vide* fig. 2, Plate IV), and there are, in consequence, numerous small foci of softening. In these foci, which are microscopic, are found ganglion cells which have undergone coagulation necrosis, lymphocytes and broken-down cell *débris* and granules. Everywhere in the cells and between the cells of the inflammatory products there are diplococci and streptococci. There are no plasma cells seen. The nerve cells show generally acute changes, some are stained dull purplish throughout, exhibit no Nissl bodies, have crumbling edges, and their dendrons destroyed. Some of the nerve cells exhibit the appearances associated with a more chronic toxic condition, viz., the perikaryon is stained diffuse pink and exhibits no Nissl bodies, whereas the outer part of the cell is stained blue from remaining Nissl bodies; the nucleus is generally pale, swollen and eccentric; the borders of the cells are curved outwards instead of incurved, and the processes are either broken off or diffusely stained.

Remarks.—I do not possess notes of this case, for beyond the statement that it was acute, no information was sent. It appears to me, however, that the acute course of the disease was due to the streptococcal invasion, firstly of the glands and secondly of the cerebro-spinal fluid and blood. The former may have been infected by the lymphatics of the nerves, and this doubtless gave rise to the acute symptoms; but, probably from the appearance of the ganglion cells and the abundant glia proliferation and perivascular mono-nuclear infiltration, there was a source of chronic irritation, non-microbial in origin. The glands show chronic changes also.

9. Bara Risgallah (male), aged 35 years; occupation, police. Lives in hut in police lines. A case which for some time had been under observation with trypanosome fever and enlarged glands. The notes state that trypanosomes were readily found in the gland juice, and they were actively motile. The stained smears show, in addition to the fully-formed trypanosomes, structures which were evidently altered trypanosomes. I am informed that acute symptoms developed and the patient died of pneumonia after ten days' illness. It was stated in the *post mortem* notes that possibly a pneumococcic meningitis would be found. The glands *post mortem* were found to contain diplo-streptococci, but not those removed *intra vitam*. Captain Greig informs me that the cerebro-spinal fluid in this case had shown mono-nuclear leucocytes.

Microscopic Examination.—A number of smear preparations of the glands were sent, and trypanosomes found. Glands removed *intra vitam* showed the following characters (*vide* figs. 3 and 4, Plate IV.).

(1) Numbers of granules, probably *débris* of cells and their nuclei, uniformly stained a dull pink; occasionally bodies which might be considered *débris* of trypanosomes and their macro- and micro-nuclei were found, and one trypanosome entire was seen (*vide* fig. 2, Plate V.).

(2) Lymphocytes in all stages of transition to the plasma cells of Marcholko can be seen. Lastly, degenerative changes of the plasma cells.

(3) Proliferated and degenerated endothelial cells.

(4) Spaces filled with deep blue stained coagulated lymph. Glands removed *post mortem* showed the same appearances, but diplococci were present.

Cerebrum, Cerebellum, Medulla Oblongata and Spinal Cord.—The meninges, especially of the cortex and base of brain and the cerebellum, were the seat of an acute pneumococcic meningitis. There was little or no perivascular infiltration with mono-nuclears; the cell exudation consisted almost entirely of polynuclears. There was no obvious glia proliferation, as seen in the other cases. Cervical spinal ganglion and nerve: Lymph spaces and lymphatics packed with cocci in great abundance. Smear preparation of spleen: No trypanosomes, granules, or micro-organisms found. Smear preparation of the centrifuged cerebro-spinal fluid: No trypanosomes; diplococci, small and large mono-nuclears, and a few red corpuscles. Smear preparation of brain: No trypanosomes found, abundance of diplococci.

Remarks.—The clinical history of this case coincides with the facts obtained by histological investigation. A chronic inflammation of the lymphatic glands associated with trypanosome infection, secondary diplococcal infection of the glands, pneumonia and pneumococcic meningitis, possibly occasioned by the defences of the organism against invasion having been destroyed by the chronic glandular affection. The absence of any obvious signs of chronic irritation of the central nervous system in the form of glia proliferation and perivascular lymphatic mononuclear infiltration may be correlated with the absence during life of any definite degree of sleeping sickness.

10. Tabula (male), aged 25. Entebbe. Occupation, marine. A chronic case of *Trypanosoma Gambiense* infection with enlarged glands, but not yet affected with signs of sleeping sickness. The lymphatic glands removed *intra vitam* exhibited inflammatory changes with necrotic foci similar to the glands of Bara Risgallah.

11. 69, L. L., and 12, 69, K. K. In both of these cases there was supuration in the deep suboccipital and cervical glands found *post mortem*, which in some cases had broken down, forming cavities. This was especially marked in the glands near the cranium (along the vessels), and those near the spinal cord. Pure cultures of diplo-streptococci were obtained from both of these cases from the cerebro-spinal fluid and heart blood.

Microscopical Examination of Brain Spinal Ganglia and Roots.—No micro-organisms were found in the brain, but abundance of diplo-streptococci in the lymph spaces of the posterior roots and spinal ganglia, also in

the blood vessels of the sheath of the ganglion, and in the lymph spaces of the nerves of neck. The perivascular mononuclear infiltration is fairly evident in the central nervous system; amidst the cells are numbers of granules of varying sizes.

13. 69. J. J. Axillary, femoral and glands of receptaculum chyli. Chronic and acute inflammatory changes, necrotic areas, diplo- and diplo-streptococci, also *Filaria perstans* in abundance.

14. 69, G. T., Masake. Admitted May 6, 1904, died May 24, 1904. Aged 16. Active trypanosomes in cervical glands. Blood also showed trypanosomes in films. No streptococci. *Post mortem* cultures from glands of neck. No streptococci.

Microscopical Examination of Tissues.—Intense chronic perivascular infiltration and glia proliferation about cerebellum and medulla (*vide* figs. 2, 3 and 4, Plate I), less obvious of cortex, very marked in cervical posterior spinal ganglia, nerves and roots. Large numbers of granules which take capsular stain. Lymphatic gland adjacent: To the naked eye (after hardening in Müller-formalin fluid), there appears to be yellow necrotic areas. Sections stained by Gram show crowds of small foci of diplo-streptococci, also in a polychrome section a transection of a vessel shows diplo-streptococci surrounded with polynuclears.

15. 69, R. R., Abimerika (male), aged 22. Admitted February 27, 1904, died June 11, 1904. The gland juice was examined on June 4, and showed active trypanosomes. No diplococci cultivated in broth and agar. *Post mortem*: No diplococci in glands. Heart's blood showed pure culture of *Bacillus coli communis*.

Microscopical Examination.—All sections of glands sent showed abundance of diplo-streptococci. Cortex, cerebellum and spinal cord show advanced chronic meningo-encephalitis, abundance of granules and occasional definite diplococci at the base of the brain; especially about the cerebellum there are foci of streptococci in the chronic inflammatory products, as if a reinfection had occurred. Transections of the blood vessels in the medulla oblongata showed a very intense perivascular infiltration, consisting of proliferated glia cells, lymphocytes, and many plasma cells and morular cells with granular *débris*. A trypanosome was seen in a transected vessel in this case. The ganglion cells have undergone profound chronic degenerative changes. This was a chronic case, and the microscopic appearances were quite in conformity, for there was marked cell degeneration and glia proliferation.

16. Sempagama (male), No. 237. Aged 8. Admitted October 10, 1903; died June 15, 1904. A very chronic case. Trypanosomes very abundant in glands, blood and cerebro-spinal fluid during life. "*Post mortem*: There was a large clot of blood over left hemisphere of brain between the dura mater and brain surface. No hæmorrhages internally. Day of death total leucocytes 74,680, polynuclears 42, and small mononuclears 43. Red blood corpuscles, 3,000,000, Hb. 70 per cent."

Microscopical Examination of Tissues.—Chronic meningo-encephalitis of brain and cord. Well marked diplo-streptococcal infection of meninges of base of brain and of the perivascular infiltration. Numerous granules, many of which take capsular stain; they lie in a sort of pink stained

amorphous substance, and it was thought that gradations between diplococci in their clear capsules to organisms which had undergone death and become merged into their capsules could be seen.

17. Case 69, K. P., Arcadi (male), aged 25. Admitted May 17, 1904; died July 27, 1904. Many trypanosomes in glands. Diplococci were obtained from glands about ten days before death. Deep cervical glands show points of suppuration.

Microscopical Examination.—Glands showed acute and chronic inflammatory changes in all the glands examined. In all the glands that were suppurating were abundant streptococci and necrotic areas, but in the glands that were not suppurating were numerous foci of diplococci. No definite trypanosomes could be seen in the sections, although frequently a body looking like macronucleus and micronucleus was seen. Pieces of *Filaria perstans* were also seen.

Chronic Meningo-encephalitis — plasma cells — glia proliferation and degeneration of the ganglion cells. Amidst the degeneration products are bodies which may be degenerated trypanosomes, also bodies which are probably dead and swollen up diplococci, and here and there can be found distinct diplococci.

18. 69, F. V., Hamesi (male), aged 12. Admitted May 5, 1904; died July 24, 1904. A rather acute case. There was a terminal streptococcal invasion, many trypanosomes in glands and blood.

Microscopical Examination.—Chronic meningo-encephalitis. Proliferation of nuclei of capillaries. Perivascular infiltration of lymphocytes, plasma cells and morular cells, with marked glia proliferation. No trypanosomes. Streptococci in the vessels and in the membranes of the pia corticalis. One lymphatic gland sent. No organisms found, but several nodules of the gland show acute inflammatory changes with many polymorpho-nuclears and coagulated fibrin.

19. 69, V. V., Wasiwa (male), aged 18. Admitted January 1, 1904; died July 22, 1904. A very chronic case. Pure trypanosome infection. No streptococcal invasion.

Microscopical Examination.—Gland taken *post mortem* contains abundance of streptococci not in blood vessels. Gland taken *intra vitam*, apparently plugs of cocci not numerous. Brain shows chronic meningo-encephalitis fairly advanced. A marked glia proliferation.

20. Dumani, male, aged 20. Admitted April 25, 1904; died May 19, 1904. Trypanosomes found in cervical glands, April 25, 1904. No streptococci.

Post mortem.—Streptococci not detected, but broken down trypanosomes in gland.

Microscopical Examination.—Glands. Plugs of diplo-streptococci in sheath of gland and especially around vessels of hilum. The gland itself does not show much change. Apparently this gland has been infected secondarily to another gland in the chain which was not sent. Degenerated trypanosomes (?). Chronic perivascular meningo-encephalitis. Miliary hæmorrhages in spinal cord. Morular cells which apparently in some instances appear to be endothelial macrophages filled with altered corpuscles (*vide* fig. 5, Plate III).

21. Case 69, Z.K., Msubika (female), aged 7. Admitted June 10, 1904, died August 12, 1904. On admission patient was in an advanced stage of the disease; she had a terminal diplo-streptococci infection. Glands were generally enlarged and in left submaxillary region showed points of suppuration.

Microscopical Examination.—Very chronic advanced meningo-encephalitis (*vide* figs. 1, 2, and 3, Plate II). To the naked eye, after hardening in formol-Müller solution the brain does not show a change like general paralysis. The cortex is of good depth, but the vessels are easily discernible, both in the grey and white matter, especially in the latter are they visible, by points and streaks of semi-translucent, grey, gelatinous appearance, with often a dark central core of blood.

The microscopic examination showed an intense meningeal and perivascular infiltration of proliferated branching glia cells, lymphocytes, plasma cells and morular cells. The cervical glands examined showed chronic inflammatory changes and although there is no suppuration in the glands examined there are abundant foci of diplo-streptococci.

Experiment 56.—Monkey (*Cercopithecus Sp.*), (*vide* p. 33. Report IV. Sleeping Sickness Commission). “To note the effect of the injection into the vertebral canal of blood containing trypanosomes from Case 66, Tabula, Marine.” April 14, 1903.—Examined blood of monkey, found malarial parasites but no trypanosomes. Injected by lumbar puncture into spinal canal 2 cc. of blood from Tabula containing trypanosomes. May 7.—Trypanosomes found in the blood of the animal. July 10.—The animal died, having shown no very marked symptoms of sleeping sickness. No temperature chart kept. The *post-mortem* examination was negative. The cerebro-spinal fluid contained living trypanosomes. “Death occurred seventy-one days after inoculation, and in our opinion is probably due to the trypanosomes.”

Microscopical Examination.—Cerebellum, cortex cerebri and medulla oblongata. No sign of meningo-encephalitis. Very marked acute chromolytic changes in the cells of the medulla, with disintegration. Some change in cells of cortex cerebri but much less pronounced. Slight change in cells of Purkinje. Nearly all the sections show malarial parasites, also diplococci and streptococci; probably a late terminal infection, as there is no evident inflammatory reaction.

Experiment 60.—Monkey (*Macacus rhesus*). “To note the effect of the subcutaneous injection of blood from a case of trypanosome fever.” April 15.—Injected subcutaneously 2 cc. of blood containing trypanosomes from Case 66, Tabula, Marine. May 7.—Trypanosomes appeared in the blood for the first time, twenty-two days after injection. May 14.—Noted as being very numerous. July 2.—Up to the present this monkey has shown no signs of being ill. To-day, however, he appears listless and less energetic. July 15.—Died. For the last fortnight the animal has presented the same picture of sleeping sickness as noted in the case of Experiment 1, monkey. Picture of the animal with its head sunk on chest. (This attitude is, however, that assumed by all monkeys when ill.—F. W. M.)

Remarks.—Page 33 Sleeping Sickness, Report IV. As far as one could judge this animal presented the typical appearances of sleeping sickness

during life, and the brain after death looks like the normal sleeping sickness brain in miniature. The organs showed no disease, so that one is bound to look upon the injected trypanosomes as the cause of death. But the trypanosomes which were injected subcutaneously into this monkey were taken from the blood of a case of trypanosome fever, Tabula, Case 66, who up to the present has shown no signs of sleeping sickness.

Microscopical Examination.—No meningo-encephalitis. A few diplococci seen by Gram's method in the brain. Nothing noteworthy in cerebrum and cerebellum except some chromatolysis of cells. It seems that the large psychomotor cells are especially deficient in Nissl granules. There is some recent glia proliferation, as shown by a comparison of the motor cortex of this animal with that of a *Macacus* that died from other causes than sleeping sickness.

Experiment 34.—"To note the effect of injecting the cerebrospinal fluid from a case of sleeping sickness into the vertebral canal of a monkey." April 8, 1903.—Injected 1 cc. of cerebrospinal fluid containing trypanosomes from a case of sleeping sickness into the spinal canal of this monkey (male, pale faced variety). April 30.—Trypanosomes appeared in blood.

Remarks.—Four months after inoculation this monkey began to show symptoms of sleeping sickness. Captain Greig writes on September 10 that the animal had died.

Post-mortem was pretty typical of an ordinary sleeping sickness case. Trypanosomes were found living in the cerebrospinal fluid of the brain.

Microscopical Examination.—No meningo-encephalitis. No perivascular infiltration. Blood vessels of brain empty. Endothelial proliferation of capillaries. Marked chromatolysis of cells of cord and medulla, to a less degree of cortex. Glia proliferation.

Experiment 8.—Monkey (*Cercopithecus Sp.*). "To note the effect of injection of blood from trypanosome fever into a monkey, and secondly, the injection of a pure culture of streptococcus from a case of sleeping sickness. The injection of blood was performed twice in April, and repeated in May, 1903. No symptoms of sleeping sickness followed; the following March (nearly a year later) subcutaneous injection of streptococcus culture. No change occurred." August 22, 1904.—It was noticed that the animal is now crouched up, and presents a dull drowsy expression. (It may be remarked that the description of the animal in no way differs from the description of the typical sleeping sickness cases.—F. W. M.) August 28.—The animal died. Trypanosomes were present in the cerebrospinal fluid, *but the fluid was sterile as regards micro-organisms.* Cysts were discovered in the liver and peritoneum, but their nature is not described.

This animal lived nearly eighteen months, apparently the *subcutaneous* injection of the streptococcus had no effect. In the remarks it states that towards the end the animal showed the characteristic signs of the disease. It is assumed that the streptococcus had nothing to do with death.

Microscopical Examination.—The cerebral cortex, medulla, internal capsule, spinal cord and cerebellum were examined. There is no perivascular infiltration or meningitis of the nervous system. There are marked chromolytic changes of the ganglion cells and some acute glia proliferation.

Experiment 99. Monkey (Cercopithecus Sp.).—"To observe the effect of infection of the monkey by tsetse flies which had fed on a sleeping sickness patient twenty-four hours previously, and the effect of subcutaneous injection of a pure culture of diplo-streptococcus on the course of this infection."

The feeding was begun on May 15, 1903.

July 23, 1903.—Trypanosomes were noted in the blood for the first time.

January 15, 1904.—Animal out of condition generally, but is still fairly active.

February 14, 1904.—Animal is weak and thin. He is crouched up, and frequently his attitude is very characteristic, the head drooping between his knees.

February 22.—Animal lies about a good deal. He takes his food better. His temperature is still swinging.

March 2.—Subcutaneous injection of pure culture of diplo-streptococcus.

March 19.—Animal is in a moribund condition. Gland in right groin distinctly enlarged; this was removed and found to contain pus. Smears showed, under the microscope, diplococci and "bodies" stained blue, which appeared to be degenerated trypanosomes.

March 20.—Animal died in the night. *Post mortem* 9 a.m. The body is markedly emaciated. Lymphatic glands in both femoral regions are enlarged. Glands in right femoral region are suppurating. Glands in axilla and neck are enlarged but not suppurating. Pupils equal and normal. No increase of fluid in pleural or peritoneal cavities, slight increase in pericardial.

Brain.—On removing the calvarium the dura mater is seen to be normal; on reflecting it, the convolutions are seen to be slightly flattened and the superficial vessels are injected; the subarachnoid fluid is increased, no active trypanosomes were seen microscopically, but the animal had been dead for some time. A pure culture of a streptococcus was obtained from the cerebro-spinal fluid.

Heart.—Nothing noteworthy. Blood from this organ examined microscopically showed many trypanosomes. Malaria is also present.

Lungs.—Both healthy.

Liver, Spleen and Kidneys.—Show nothing noteworthy.

Intestines.—Healthy.

Lymph Glands.—In omentum and mesentery distinctly enlarged.

Remarks.—This experiment demonstrates several points of importance, the first being that it is possible to convey the trypanosma of sleeping sickness from man to monkey after an interval of twenty-four hours; secondly, that the disease produced in the monkey by the fly infection presents the same characters as that produced by inoculation of cerebro-spinal fluid or blood from a case of sleeping sickness. This animal presented towards the close of its life a typical picture of a sleeping sickness case.

The experiment is, finally, of interest and importance from the fact that fifteen days before its death it had been injected with a pure culture of diplococci obtained from a case of sleeping sickness. So far as we could observe, the course of the disease was uninfluenced by the injection, the

only noteworthy feature being a slight suppuration in one of the groups of lymphatic glands near the seat of inoculation. Portions of the nervous system and glands have been preserved for minute investigation and the results of the examination will be of interest. (Sleeping Sickness, Report VI., p. 39.)

Microscopical Examination.—In the medulla, cord and brain there was no trace of perivascular infiltration or meningitis found. There was a little chronic inflammatory thickening at one spot of the floor of the 4th ventricle. The marked ehromolytic and acute destructive changes found in the spinal cord and medulla of an uneven nature was very striking and resembled the changes seen in Surra rabbit (p. 22) and Jinga trypanosomiasis of ox. In the cord and medulla oblongata also a few capillary hæmorrhages were seen, but a careful search showed no flagellated organisms in the blood contained in the vessels of the central nervous system. Appearances, however, were presented closely similar to those met with in Jinga trypanosomiasis, viz., the capillaries both in transverse and longitudinal section showed oval and round protoplasmic bodies stained pink, measuring from 4 to 10 μ , which contained minute chromatin particles in varying numbers and sizes. In many instances these bodies could be seen lying in the lumen of vessels transversely and longitudinally, also free in the brain tissue. The chromatin particles frequently had the appearance of rings measuring 1 μ and other small particles were frequently seen in the pink stained protoplasm. Those lying in the wall of the vessel or outside it might be proliferated and swollen endothelial or glia cells. Examination of a blood film did not show these bodies although a few trypanosomes were found. There is pronounced glia cell proliferation in the cortex cerebri, especially in the subjacent white matter; also in the cerebellum. The cells are probably young for they have as a rule, few and not extensive branching processes and the cell protoplasm is proportionally scanty.

Experiment 228, p. 106. Reports, Vol. VI. of Sleeping Sickness Commission: Monkey (*Cercopithecus Sp.*).

“To note the effect of the trypanosome carried by tsetse flies freshly caught in the vicinity of Entebbe on a monkey.”

The experiment was started on October 12 and a large number of flies fed on the animal, but it was not until November 26 that trypanosomes were found in the blood. After this no more flies were fed on the animal and it lived until June 19, when it was in a moribund condition and was killed by chloroform. The brain presented no noteworthy naked eye change. The superficial lymphatic glands, both femoral and axillary were enlarged; abdominal slightly enlarged.

Remarks.—This experiment illustrates the course of the disease produced by the trypanosomes carried by the tsetse flies (*Glossina palpalis*) freshly caught in the vicinity of Entebbe. It closely resembles the experiment in which the *Trypanosome Gambiense* was injected into the monkey. In both the course of the disease was a *prolonged* one; the animal in this experiment also showed definite signs for some time before death. At times it presented the characteristic features met with in the sleeping sickness monkeys. The temperature curve was also very similar. This experiment supports the

view that the trypanosome carried by the freshly caught tsetse fly in Uganda is identical with the *T. Gambiense*.

Microscopical Examination.—Portions of the brain and medulla were examined. There was no obvious perivascular cell infiltration, but there was a very marked chromolytic change of the ganglion cells of the medulla, somewhat similar to that seen in the Surra rabbit's brain. A considerable degree of acute glia proliferation, especially marked in the subjacent cortical white matter, also in the medulla oblongata (*vide* fig. 1, Plate III).

There is a perivascular glia proliferation especially about the smaller vessels. These cells are larger than normal, star-like, and show many branching processes, extending on to the vessels. A portion of the cervical enlargement of the spinal cord with anterior and posterior roots attached, also posterior spinal ganglion and three quarters of an inch of the cerebro-spinal nerve beyond the ganglion with adherent tissue was embedded in paraffin and cut in one block. The sections were stained by the various methods described and microscopical examination proved of considerable interest. The adherent connective tissue attached to and forming part of the sheath of the cerebro-spinal nerve shows a chronic inflammatory change similar in many respects to that observed in the lymphatic glands and perivascular lymphatics of the central nervous system in human sleeping sickness. There is a marked proliferation of the endothelial cells with nuclear proliferation and endogenous nuclear changes, degeneration and necrosis of the cytoplasm of the cells and lymphocyte accumulation. Stained by Gram method no micro-organisms were seen. Stained for trypanosomes, the appearances were exactly like those observed in the lymphatic glands removed during life (and in which active living trypanosomes were found in the juice), viz., occasional appearances which may be due to modified or degenerated trypanosomes. Since this chronic inflammation does not appear to have been caused by microbial invasion and as undoubtedly this animal was infected by the flies with trypanosomes we may conclude that this chronic inflammation of the adjacent structures and sheath of the nerve was due to the trypanosomes (fig. 3, Plate IX).

If the nerve be traced from this inflammatory perineural tissue to the ganglion, small accumulations of lymphocytes can be observed in the lymph spaces, and there is an early interstitial nuclear proliferation in the spinal ganglion, but this is only obvious in scattered places. Along the posterior roots there are small scattered accumulations of lymphocytes, but on reaching the spinal cord there is some evidence of chronic irritation by the sub-pial and septal proliferation of the neuroglia tissue. This is most obvious at the ring where the posterior root fibres enter the posterior horn; it extends on the lateral surface, nearly halfway to the anterior median fissure and posteriorly to the posterior median fissure. There is slight proliferation but not so marked in the remainder of the periphery of the spinal cord (*vide* photomicrograph). This distribution suggests that the noxious agent is carried especially by the lymphatics of the posterior roots. There appears to be a commencing glia proliferation of the grey matter generally, but this is not so obvious.

The neuroglia change in this cord closely corresponds with that observed

by me in the lumbo-sacral region of a horse that died of Dourine (*Trypanosoma equiperdum*).

These observations tend to show that the lymphangitis may extend from the lymphatic glands of the neck along the perineural lymphatics, but prior to this a noxious irritative agent may be absorbed by the neural lymphatics and bring about a neuroglia proliferation. There appears to be an excess of lymphocytes in the grey matter, and here and there accumulations of lymphocytes around the small vessels can be seen. Unless all the lymphatic glands of the body can be proved to be free from microbial infection—consequently absorption of microbial toxins by the neural lymphatics put out of court as a cause of this chronic glia irritation and proliferation—it may always be considered as not proved beyond all shadow of doubt that the trypanosome infection *per se* is the cause.

BIBLIOGRAPHY.

- ¹ MOTT. "The Changes in the Central Nervous System of Two Cases of Negro Lethargy, sequel to Dr. Manson's Clinical Report," *Brit. Med. Journal*, vol. vi. p. 1666, 1899.
- ² MOTT. "A Case of Negro Lethargy, by Stephen Mackenzie, with a Note on the histological Changes of the Nervous System by F. W. Mott," *Trans. Path. Soc. Lond.*, vol. li., part ii., 1900.
- ³ MANSON and MOTT. "African Lethargy, or the Sleeping Sickness," *Trans. Path. Soc. Lond.*, vol. li., part ii., 1900.
- ⁴ MOTT and LOW. "The Examination of the Tissues of a Case of Sleeping Sickness in a European," *Brit. Med. Journal*, April, 1904.
- ⁵ MOTT. "Observations on the Brains of Men and Animals Infected with Various Forms of Trypanosomes," *Proceedings of the Royal Society*, vol. B. 76, 1905.
- ⁶ MOTT. "The Cerebro-spinal Fluid in Relation to Diseases of the Nervous System," *Brit. Med. Journal*, December, 1904.
- ⁷ BETTENCOURT. Kopke, Gomez de Rezende, Correa Mende, "La Maladie du Sommeil," Lisbon, 1903.
- ⁸ WARRINGTON. "A Note on the Condition of the Central Nervous System in a Case of African Lethargy," *Brit. Med. Journal*, vol. ii, p. 929, 1902.
- ⁹ SICARD et MONTIER. "Recherche Bact. et Histol. dans un cas de Maladie du Sommeil chez un blanc," *La Presse Med.*, December, 1905.
- ¹⁰ CASTELLANI. "Researches on the Etiology of Sleeping Sickness," *Journal of Tropical Medicine*, June, 1903.
- ¹¹ BRUCE. "Reports of the Sleeping Sickness Commission."
 - Vol. I. (1) CASTELLANI. "Presence of Trypanosomes in Sleeping Sickness."
 - (2) BRUCE and NABARRO. "Progress Report on Sleeping Sickness in Uganda."
 - Vol. II. (3) CHRISTY. "The Distribution of Sleeping Sickness."
 - (4) CASTELLANI. "Adult Forms and Developmental Forms of the Trypanosomes found in Sleeping Sickness."
 - (5) LOW and CASTELLANI. "Report on Sleeping Sickness from its Clinical Aspects."
 - Vol. III. (6) CHRISTY. "The Epidemiology and Etiology of Sleeping Sickness in Equatorial East Africa."
 - (7) THEOBALD. "Report on a Collection of Mosquitoes and other Flies from Equatorial East Africa."

- Vol. IV. (8) BRUCE, NABARRO and GREIG. "Further Report on Sleeping Sickness in Uganda."
- Vol. V. (9) AUSTEN. "A Provisional List of Diptera."
 (10) NABARRO and GREIG. "Further Observations on the Trypanosomiasis (Human and Animal) in Uganda."
- Vol. VI. (11) GREIG and GRAY. "Continuation Report on Sleeping Sickness in Uganda."
 (12) GREIG. "Report on Sleeping Sickness in the Nile Valley."
 (13) AUSTEN. "The Distribution of Tsetse-flies."
 (14) GRAY and TULLOCH. "The Multiplication of the Trypanosoma in the Alimentary Canal of the Glossina Palpalis."
- ¹² THOMAS and ANTON BREINL. "Trypanosomes, Trypanosomiasis and Sleeping Sickness. Report vol. vi., part ii., 1905." Thompson Yates and Johnston Laboratories, University of Liverpool.
- ¹³ NOVY. *Journal of Infectious Diseases*, vol. ii., No. 2, March, 1905.
- ¹⁴ KOPKE. "Investigações sobre a Doença do Somno," *Archivos de Hygiene e Pathologia Exoticas*, vol. i., fasc. 1.
- ¹⁵ HARVEY. "Report on a Case of Experimental Sleeping Sickness in a Monkey," *Journal Royal Army Medical Corps*, May, 1905.
- ¹⁶ BRADFORD and PLIMMER. "The Trypanosoma Brucei, the Organism found in Nagana or Tsetse-fly Disease," *Quart. Journal Micro. Science*, vol. xlv., April 20, 1905.
- ¹⁷ ROGERS. "Preliminary Note on the Development of Trypanosoma in Cultures, of the Leishman Donovan Bodies of Cachexial Fever and Kala Azar," *Lancet*, July 23, 1904.
- ¹⁸ MARSHALL. The present state of knowledge is well summed up by Marshall (F. W. M.). "Trypanosomiasis or Sleeping Sickness," *Review of Neurology and Psychiatry*, February, 1906.
- ¹⁹ JOLLY, M. J. "Sur les Mouvements des Lymphocytes," *Soc. de Biol.*, June, 1902.
- ²⁰ ALZHEIMER. "Histologische Studien zur Differenzialdiagnose der Progressiven Paralyse."
- ²¹ PLIMMER. "Note on the Effect produced on Rats by the Trypanosomata of Sleeping Sickness," *Proceedings of the Royal Society*, vol. lxxiv., No. 504, February 24, 1905, pp. 388-390.

DESCRIPTION OF PLATES.

Except where otherwise stated all sections were stained with methylene blue and eosine.

PLATE I.

FIGS. 1-4.—Appearances presented by the vessels of the brain in a very chronic case of sleeping sickness.

FIG. 1.—Transection of small vessel of medulla oblongata, showing perivascular infiltration with hyaline lymphocytes. In the centre of the blood vessel is a trypanosome (*t*). Amidst the blood corpuscles there are numerous small and large mononuclear leucocytes (*mon. l.*). Magnification 500.

FIG. 2.—Small vessel, with plasma cells (*p*) and large granule cells, which I have termed morular cells (*m*). They correspond to Körnchen Zellen of Alzheimer. Magnification 500.

FIG. 3.—Small vessel dividing into two capillaries, showing nuclear proliferation of the endothelial cells; in the neighbourhood are plasma cells (*p*), lymphocytes (*l*), and glia cells (*g*). Magnification 500.

FIG. 4.—Section of spinal ganglion, showing lymphocyte interstitial infiltration (*l*). Magnification 120. Same section is shown more highly magnified in fig. 1, Plate VII.

PLATE II.

FIG. 1.—Three large glia cells (*g*), their branches ending in a network around and upon a small vessel; lymphocytes (*l*), and plasma cells (*p*) are seen scattered about. Magnification 500.

FIG. 2.—Small vessel, showing endothelial nuclei proliferated, and three plasma cells. Magnification 500.

FIG. 3.—A transection of a vessel in a very chronic case of sleeping sickness, showing marked perivascular infiltration. Magnification 250.

FIG. 4.—Active proliferating young glia cells found in great numbers in sleeping sickness tissues. The pale nucleus, with distinct nuclear membrane, contains chromatin granules, with an arrangement indicating mitosis. Surrounding the nucleus is the pink-stained cytoplasm, with a tendency to form star-like processes. Magnification 500.

FIG. 5.—Two large morular cells from a very chronic case of sleeping sickness. Magnification 500.

FIG. 6.—Rod cells (Stäbchen Zellen) are rarely met with, although occasionally appearances like fig. 6 are seen. Magnification 500.

PLATE III.

FIG. 1.—Section of subcortical matter of brain of monkey that died after infection by trypanosomes caused by infected flies being allowed in considerable numbers to bite the animal. Experiment 228. There is little or no perivascular lymphocyte infiltration, but a considerable increase in size and number of the perivascular glia cells. Magnification 430. Stained by Heidenhain method.

FIG. 2.—Section of subcortical white matter of monkey that died eighteen months after infection and which showed the characteristic lesion of sleeping sickness. Harvey and Leishman. The glia proliferation is well seen, and in the meshwork of the branching fibres which form the reticulum of the perivascular lymphatic space (which is seen in longitudinal section) are numerous lymphocytes. The body and reticulum of the glia cells are stained pink in the section; the lymphocytes and neuroglial nuclei are stained blue. Magnification 600.

FIG. 3.—Transection of a blood vessel in the sub-cortical white matter—sleeping sickness. Only the neuroglial nuclei are stained. The lymphocytes are pale and unstained, and lie in the branching meshwork of the glia cells. Magnification 480. Eosin's stain.

FIG. 4.—Small vessel of brain of monkey in which the blood vessels of the brain had been rendered empty, and collapsed by ligation of all four arteries. This is to show the perivascular space filled with cerebro-spinal fluid, and the supporting neuroglial trabeculae; such as are shown in the drawing are only seen at intervals. It can be understood that if these trabeculae are greatly increased the lymphocytes will tend to be caught in the meshes. Magnification 500.

FIG. 5.—Shows macrophages (a) containing blood corpuscles, the result of a hæmorrhage into the cerebro-spinal cavity; lymphocytes (b), and diplococci (c), which are undergoing lysis. In the immediate neighbourhood could be seen crowds of diplococci and diplo-streptococci, which stained deep blue. Magnification 500.

FIG. 6.—Vessel of the brain with bacilli. Case 7, p. 30. Magnification 500.

PLATE IV.

FIG. 1.—Transection of cervical nerve close to the spinal ganglion, showing an infection of the sheath of the nerve by diplo-streptococci. The adjacent lymphatic glands showed points of suppuration. Magnification 200. (a) The micro-organisms, magnified 500. Case 69, L.L.

FIG. 2.—Vessel of the internal capsule of a case of acute sleeping sickness, with a large plug of cocci. Magnification 500. Stained by Gram's method.

FIG. 3.—Various degenerated cells seen in section of sterile lymphatic gland. Magnification 1,000. Leishman stain.

FIG. 4.—Lymphocytes and their transition to plasma cells *a, c*; *d*, degenerated plasma cell seen in section of lymphatic gland. Magnification 1,000. Leishman stain.

PLATE V.

FIG. 1.—Thread-like bodies and granules deeply stained, seen in section of lymphatic gland, probably altered and degenerated trypanosomes. Magnification 1,000.

FIG. 2.—Trypanosome in a lymphatic gland section amidst disintegrated cell products. Figs. 3 and 4 (Plate IV.), and figs. 1 and 2 (Plate V.), are drawings made from the same sections, 5 μ in thickness, stained with Leishman's stain and prepared from an enlarged cervical gland removed during life from a case (Bara Risgallah) of trypanosome fever, before symptoms of sleeping sickness had occurred. Magnification 1,000.

FIG. 3.—*Trypanosoma Gambiense* in smear of fresh gland juice, several lymphocytes, micro-nuclei. Magnification 1,000.

FIG. 4.—Section of lymphatic gland from a recently fatal case of sleeping sickness in a European. The glands in this case were not much enlarged. There is a very marked proliferation of the endothelial nuclei. Magnification 500.

FIG. 5.—Proliferation of the connective tissue cells of the reticulum of a lymph sinus; marked proliferation of the nuclei of the endothelial cells seen. This chronic change closely accords with the change observed in the perivascular lymph spaces of the central nervous system. Magnification 500.

FIG. 6.—Various granules and products of cell (and trypanosome?) degeneration seen in the perivascular infiltration of the central nervous system in sleeping sickness. Magnification 1,000.

PLATE VI.

Appearance of various pyramidal cells of the cerebral cortex in cases of very chronic sleeping sickness, showing various stages of chromatolysis and chronic degeneration. One cell is covered with phagocytes (*h*). Magnification 500.

PLATE VII.

FIG. 1.—Same section as that on Plate I., 4, more highly magnified, showing endothelial cell proliferation of the capsules of the posterior spinal ganglion cells and interstitial lymphocyte infiltration. Magnification 500.

- FIG. 2.—Filum preparation of *Jinga* trypanosoma in blood of infected monkey. Two trypanosomes are seen and three blood corpuscles. Beside there is a body, which appears as if fission were about to occur. Magnification 1,000.
- FIG. 3.—Transection of a vessel of brain of ox that died of *Jinga* trypanosomiasis a short time after inoculation. A large number of chromatin rings are seen. Magnification 1,500.
- FIG. 4.—Longitudinal section of a vessel of the same. Magnification 1500.
- FIG. 5.—Bodies seen in a vessel of brain of ox. Some modified form of trypanosome? Magnification 1,000.
- FIG. 6.—Splenic blood smear, showing Leishman Donovan bodies. Case of Kala-Azar somewhat similar appearance to 5. Magnification 1,000.
- FIG. 7.—Spleen Kala-Azar, showing Leishman bodies in the form of definite chromatin rings. Note the similarity to the appearance presented by 3, 4 and 5. Magnification 1,000. Stained by Van Gieson's method.

PLATE VIII.

- FIG. 1.—Longitudinal section of vessel of brain of ox that died of *Jinga* infection. Trypanosomes in various modified shapes are seen. Some of these may be amœboid forms of trypanosomes; probably some are trypanosomes which have been attacked by leucocytes. Magnification 500. Stained in bulk—methylene blue and eosine.
- FIG. 2.—Small vessel of the medulla oblongata of rabbit inoculated with Surra. The animal died three months after infection. Shows a plasmodial mass in the centre and trypanosomes in a whorl near by. Magnification 1,000. Polychrome.
- FIG. 3.—Nerve cells of above, showing chromatolysis, and a small vessel with the trypanosomes (*t*) coiled up, blocking it. Magnification 1,000. Polychrome.
- FIG. 4.—Somewhat similar appearances as in fig. 2, seen in longitudinal section of vessel. Numbers of chromatin rings, probably macro-nuclei (A); (B) capillary blocked by trypanosomes; (C) trypanosomes in the tissue; (D) ganglion cell, showing marked chromolytic changes, probably due to capillary obstruction. The nucleus is swollen and clear, the body of the cell shrivelled, and there is an absence of Nissl granules. Magnification 1,000. Romanowsky.

PLATE IX.

- FIG. 1.—Section of cortex showing pyramidal ganglion cells of Meynert's columns. It will be observed that the cells stain well, have retained fairly well a normal shape, and, considering the thinness of the section $5\ \mu$, their numbers are not appreciably diminished. The lymphocyte and glia cell infiltration is not prominent in this region, although the specimen was made from the brain of a case of advanced sleeping sickness (Sempagama, Case 16, p. 33). Magnification 185.
- FIG. 2.—Section of the cortex of a case of advanced sleeping sickness stained by Weigert method, to show condition of fibres. It will be observed that there is no gross fibre atrophy. Under a high power there is a diminution in some places, considerable of the tangential fibres and, to a less degree, of the super radial. Magnification 50.
- FIG. 3.—Section of the spinal cord of Monkey 228. This animal died eight months after infection by fresh fly feeding. Observe the increase in number and size of the glia cells in the posterior column close to the posterior horn. There is also an accumulation of lymphocytes close to the ring of entry of the posterior root. These are seen somewhat indistinctly, owing to their being massed together. Magnification 170.
- FIG. 4.—Section of spinal cord of very chronic sleeping sickness (Droya, Case 6, p. 29). It shows no coarse tract degeneration, but under a higher magnification the most extensive subpial, septal and universal neuroglia proliferation can be seen. Magnification 7.
- FIG. 5.—The neuroglial septal proliferation.

PLATE X.

FIG. 1.—Central canal of 1st cervical segment of spinal cord, showing proliferation of ependymal cells to form glia cells. As the proliferation proceeds from within outwards, the ring of new young cells increases, leaving a more fibrillary substance behind in the centre, which fills up the canal. Around the ring of cells there is also a zone of a more fibrillary substance. The fibrils are the processes of the glia cells. Magnification 90.

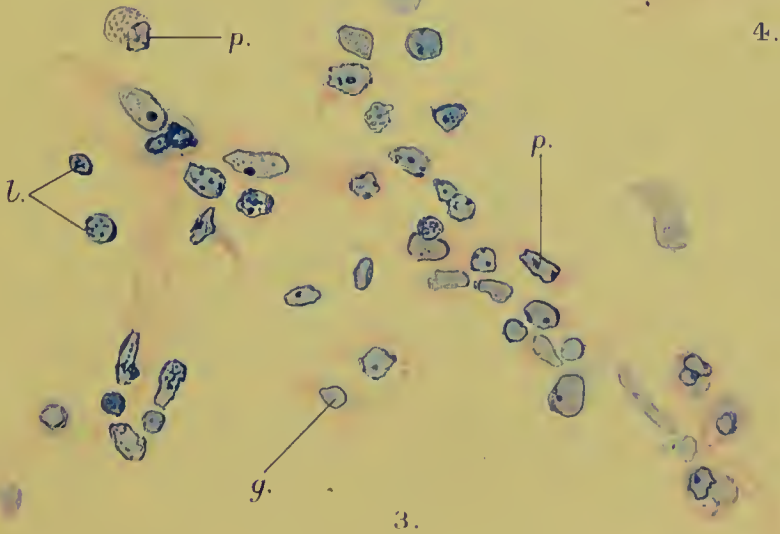
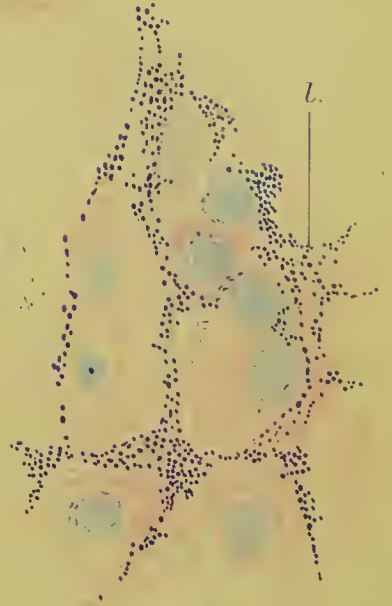
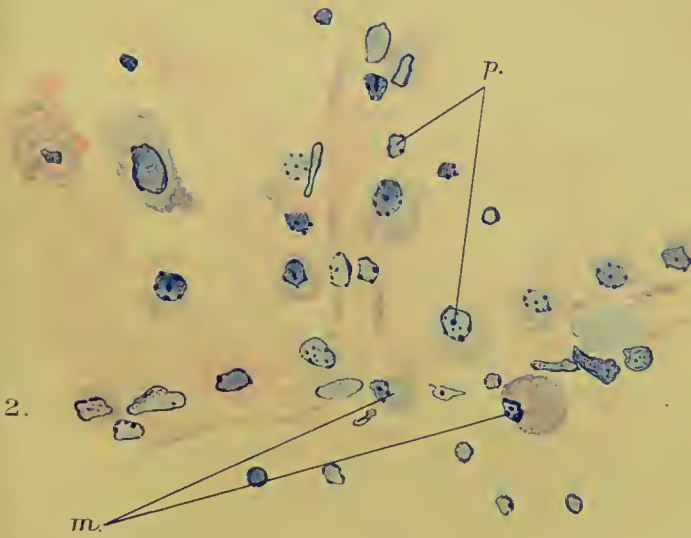
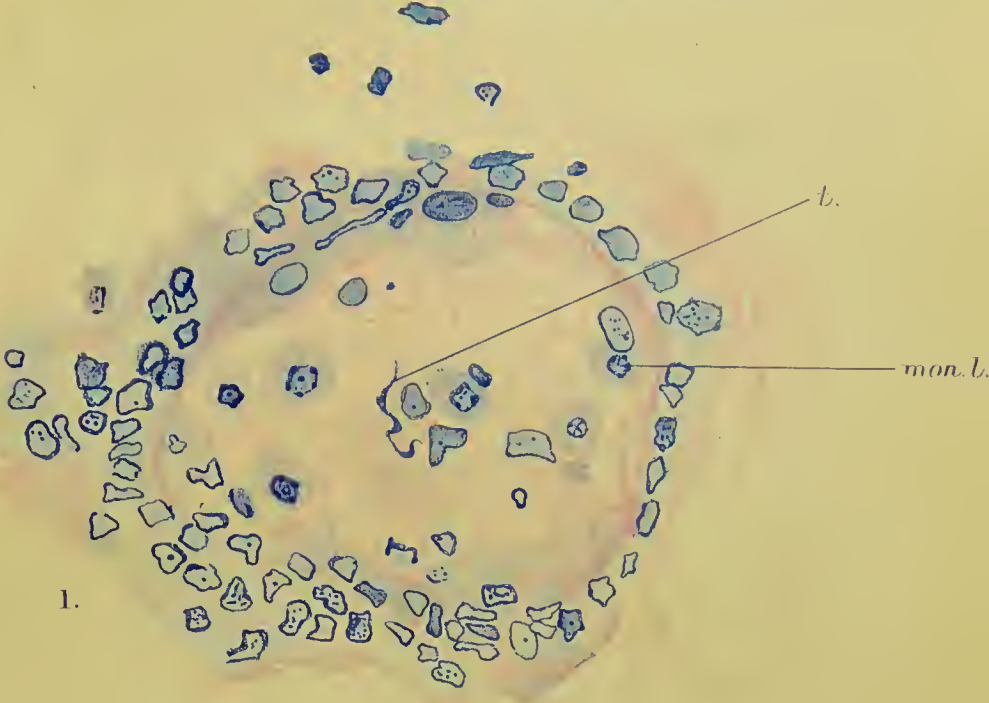
FIG. 2.—Section of the heart of a case of advanced sleeping sickness which shows an accumulation of lymphocytes in the intermuscular lymph spaces. Magnification 250.

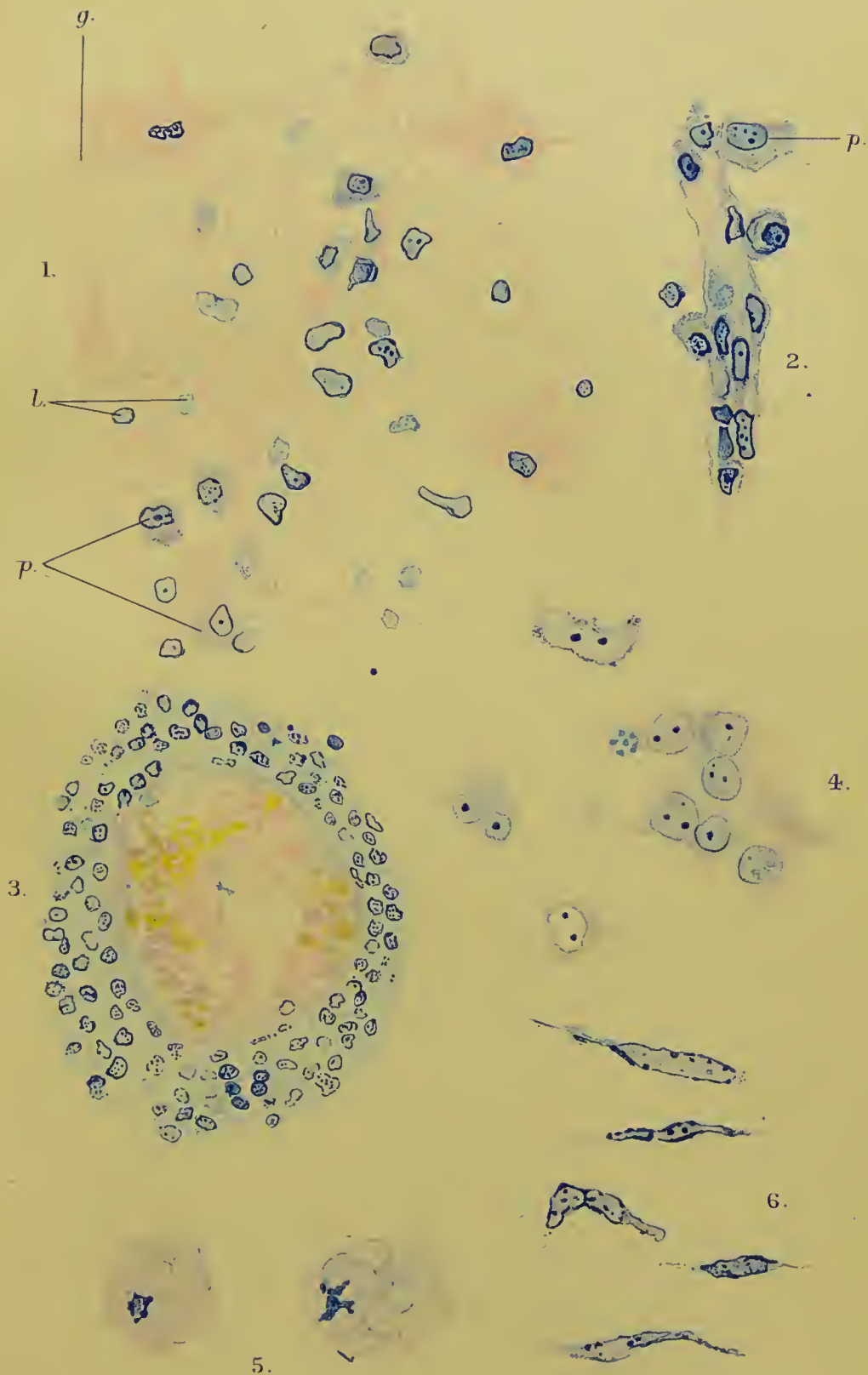
FIG. 3.—Section of the liver showing a chronic interstitial inflammatory change. There is accumulation of lymphocytes in the lymph channels of the portal canal. Magnification 180.

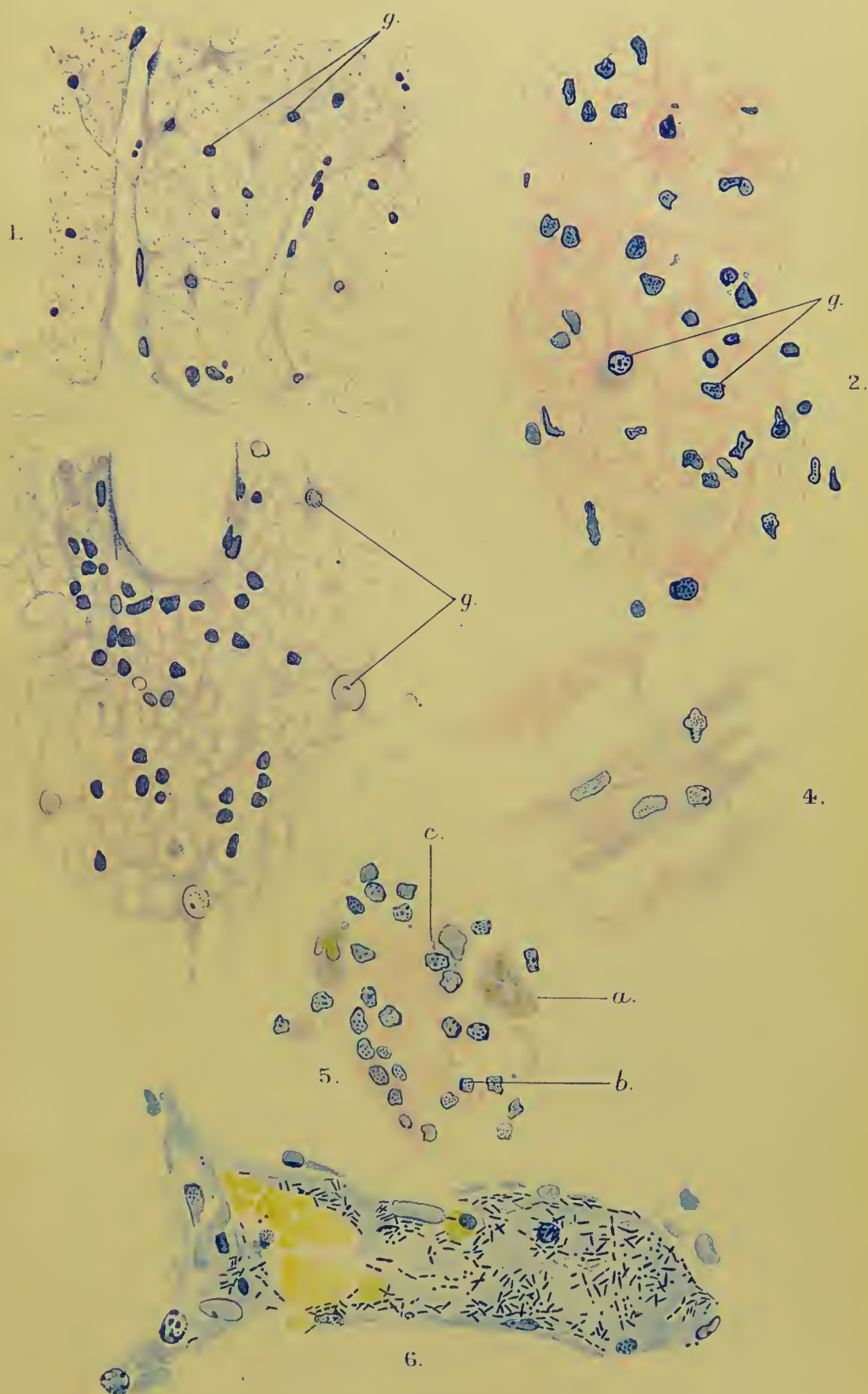
FIG. 4.—Anterior horn cell from a case of advanced sleeping sickness. The cell takes the basophile stain well, the Nissl granules are abundant in the body of the cell and on the dendrons. The cell infiltration around is mostly neuroglia, but there are lymphocytes. Magnification 540.

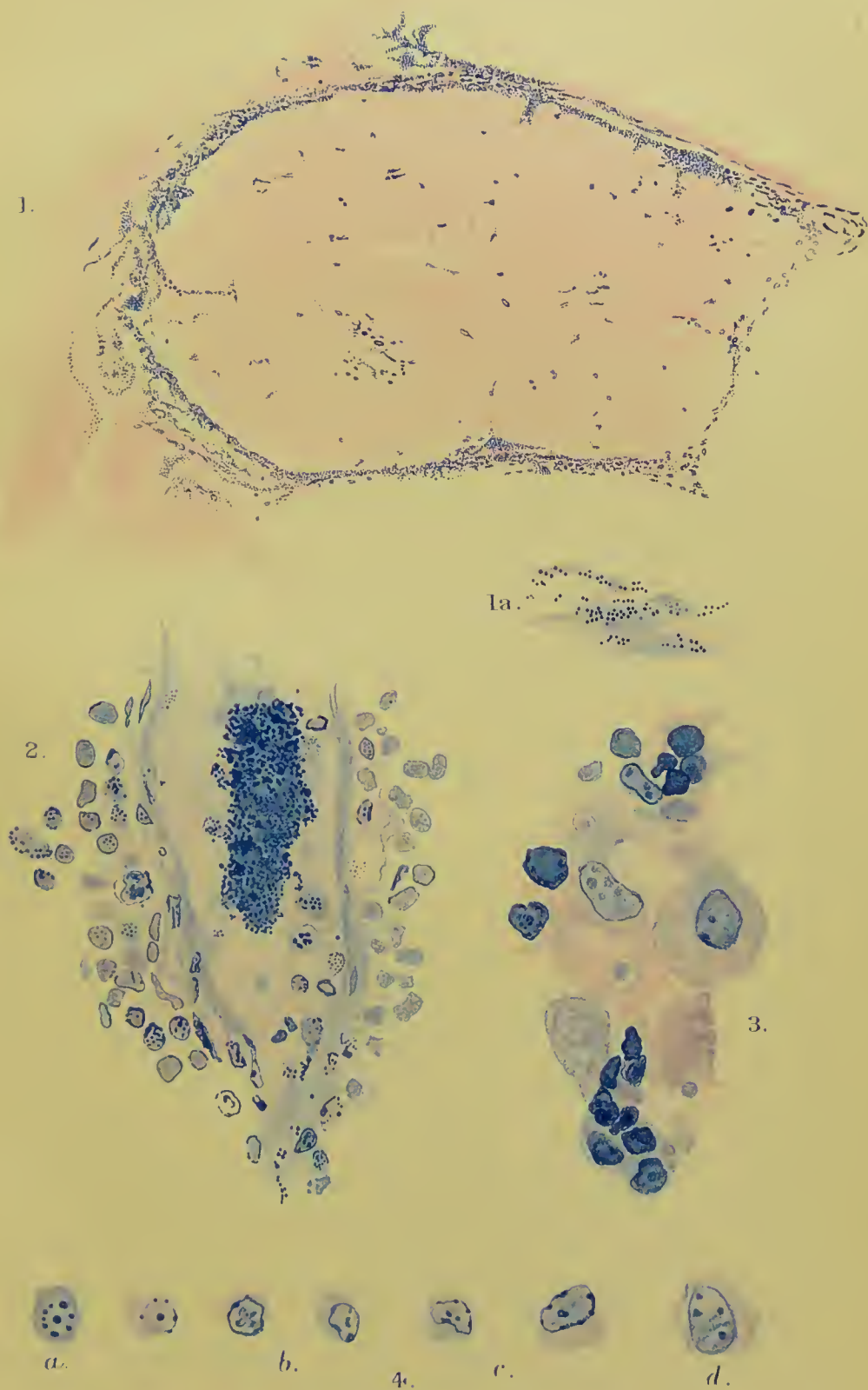
PLATE XI.

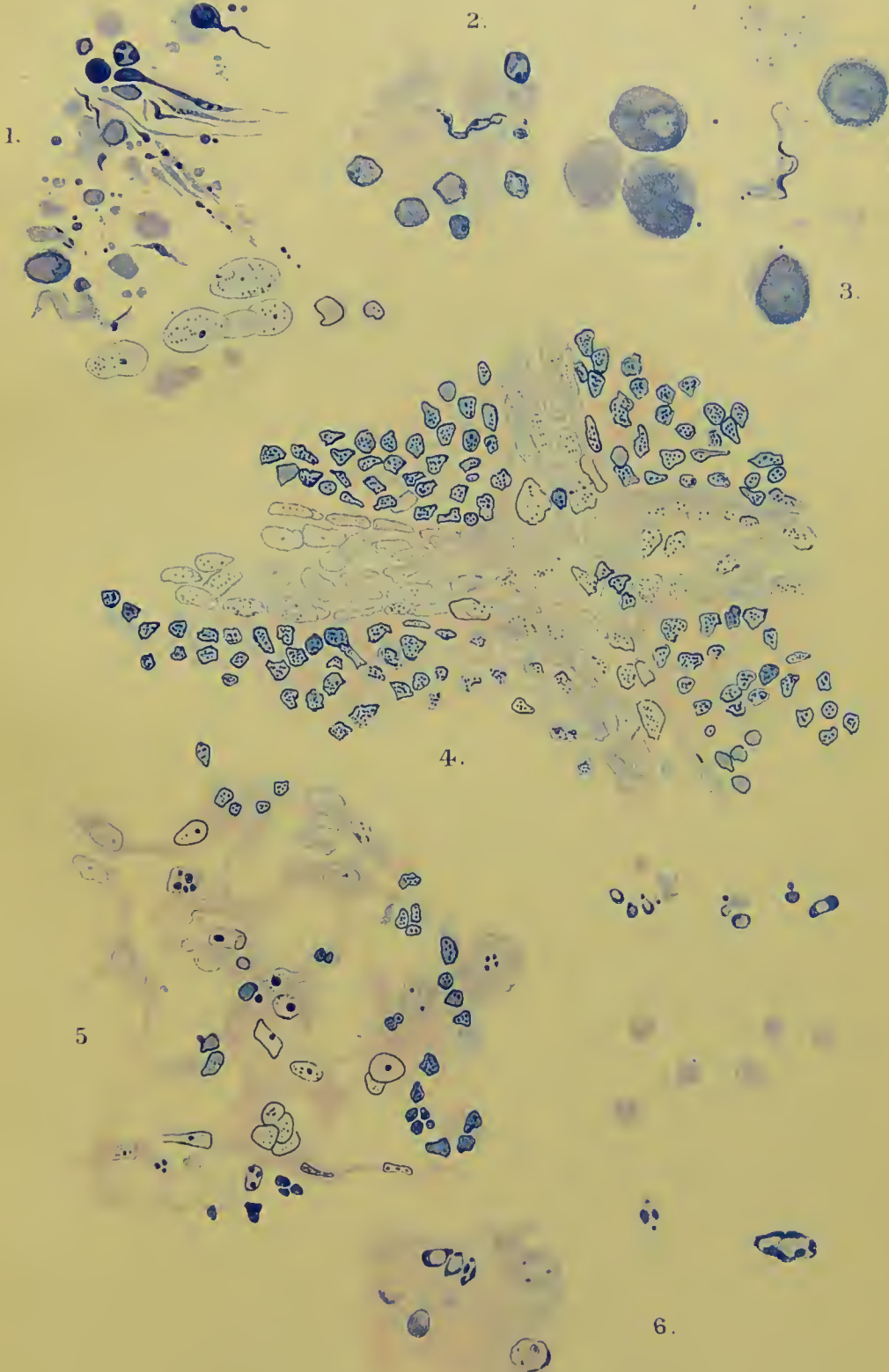
Photographs of two Sleeping Sickness Patients (see Appendix, pp. 29-30).

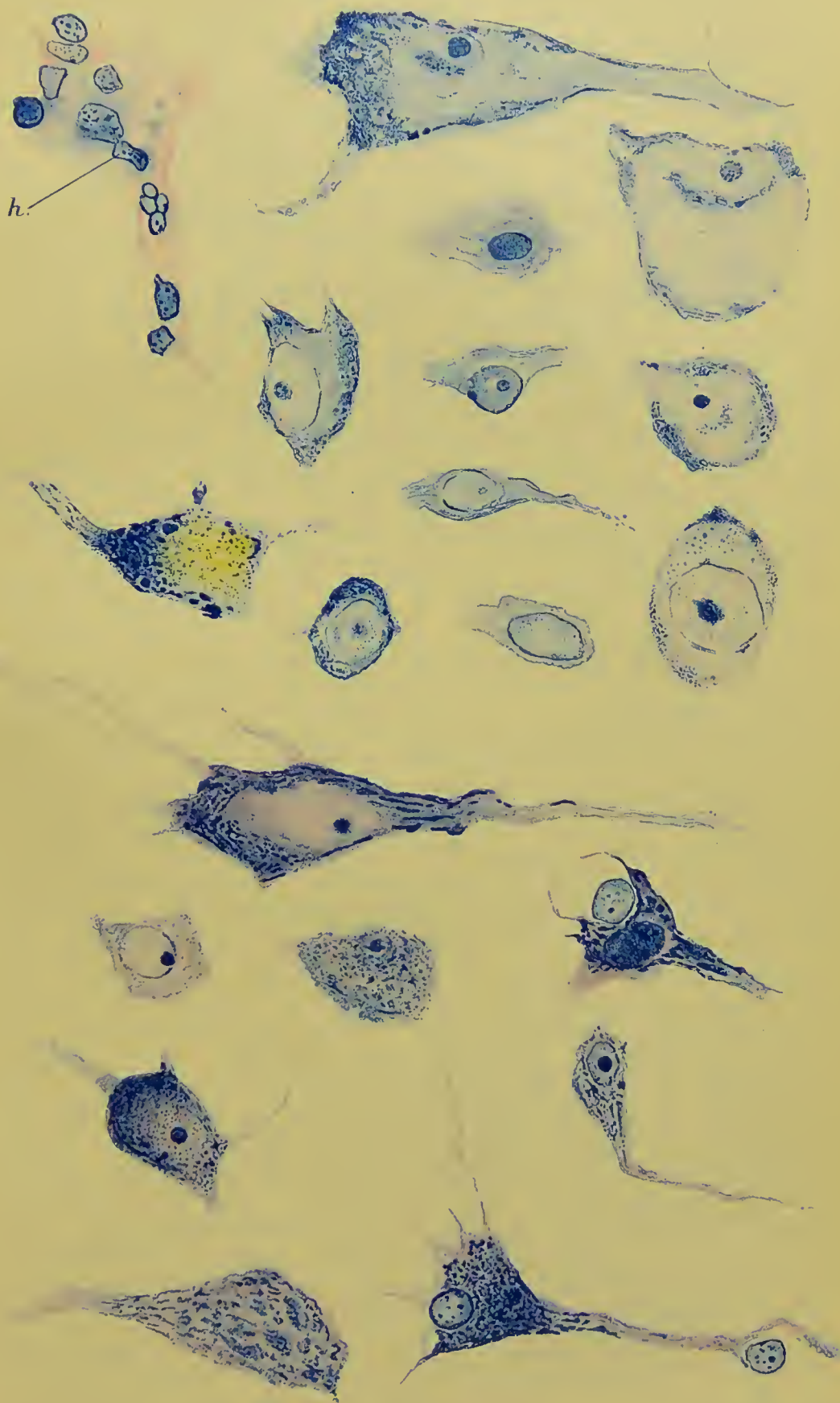












1.

2.

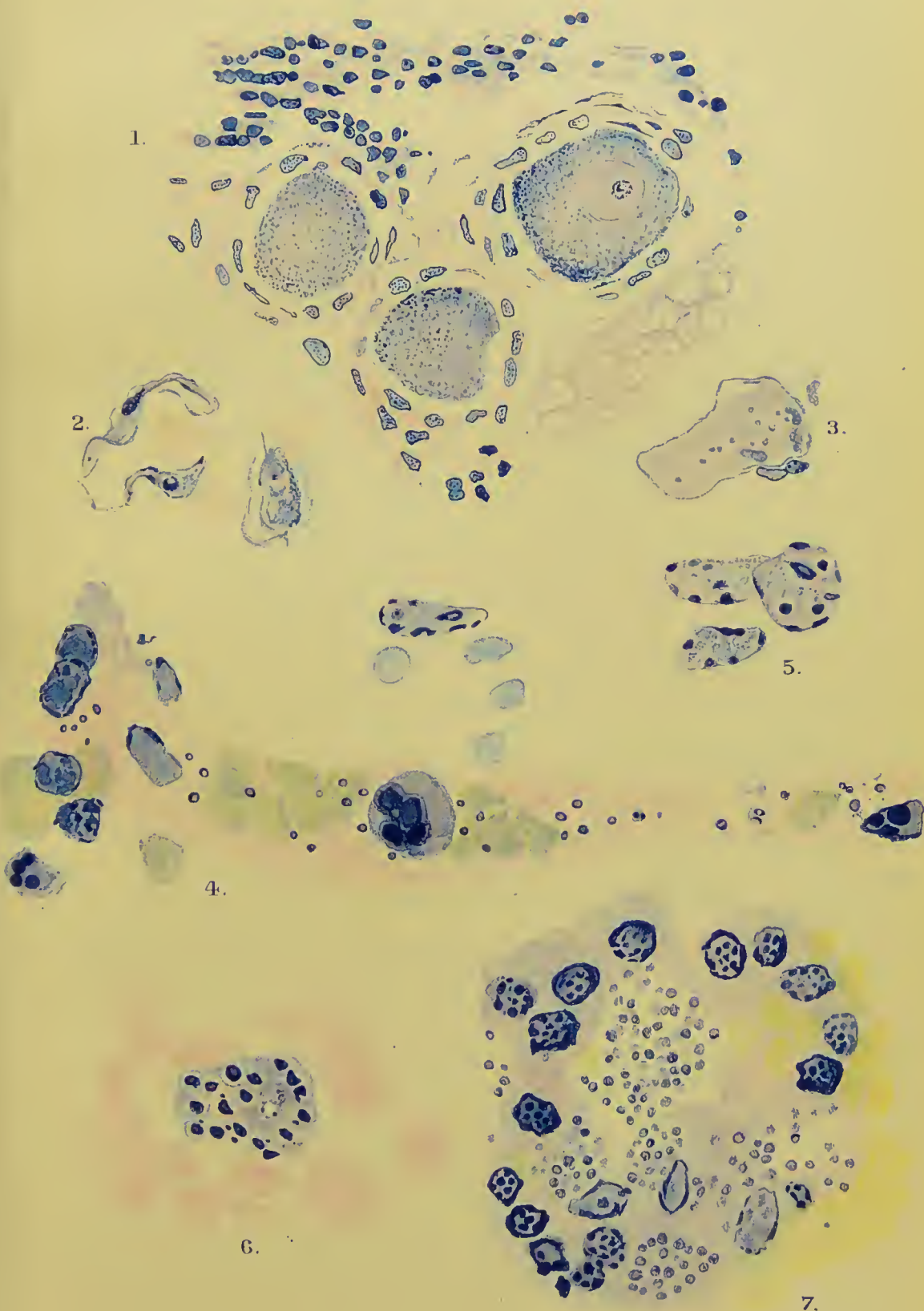
3.

5.

4.

6.

7.



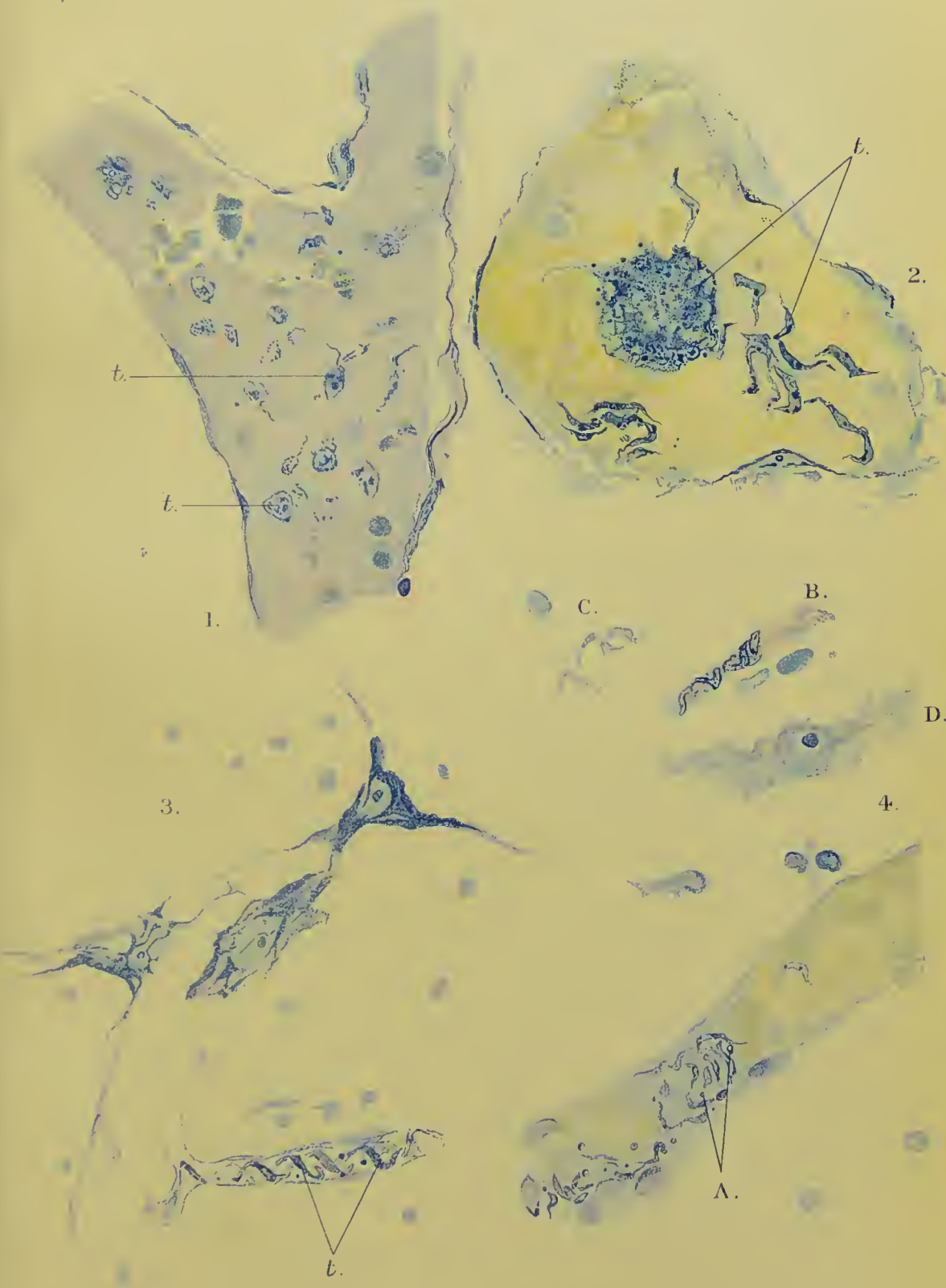




FIG. 1.

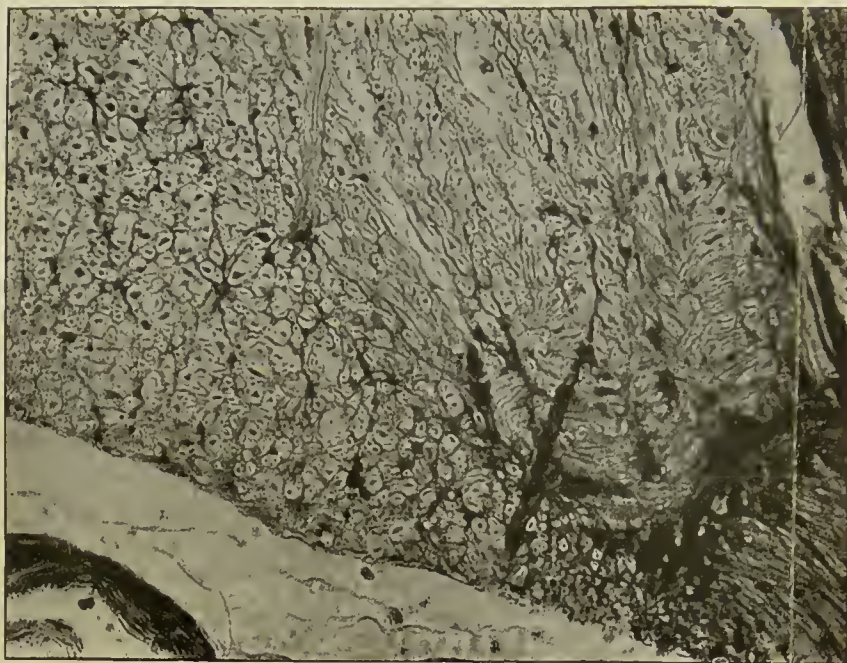


FIG. 3.



FIG. 4.



FIG. 2.

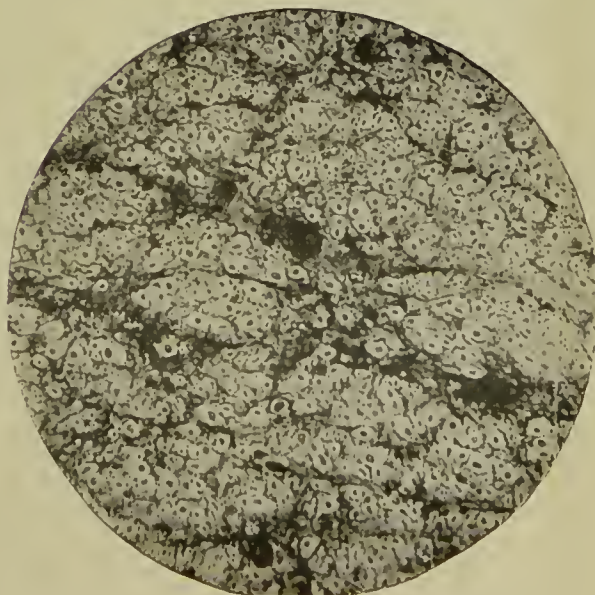


FIG. 5.



FIG. 1.

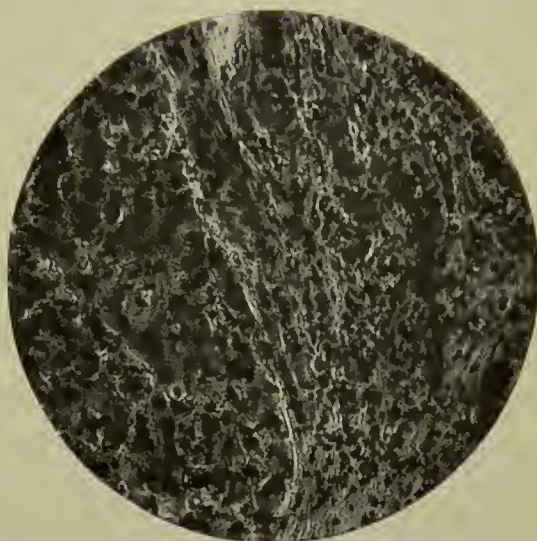


FIG. 3.

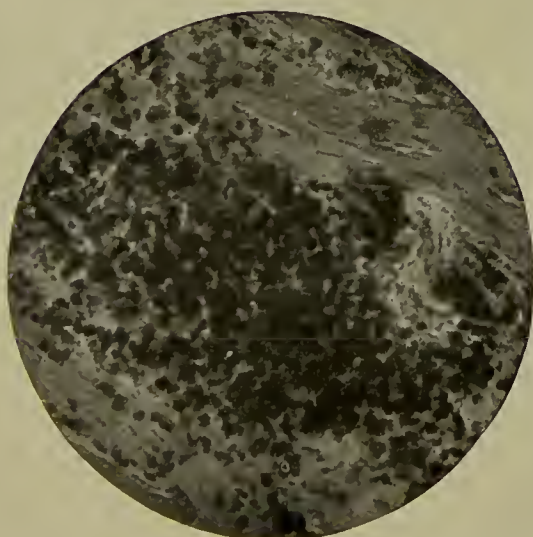


FIG. 2.

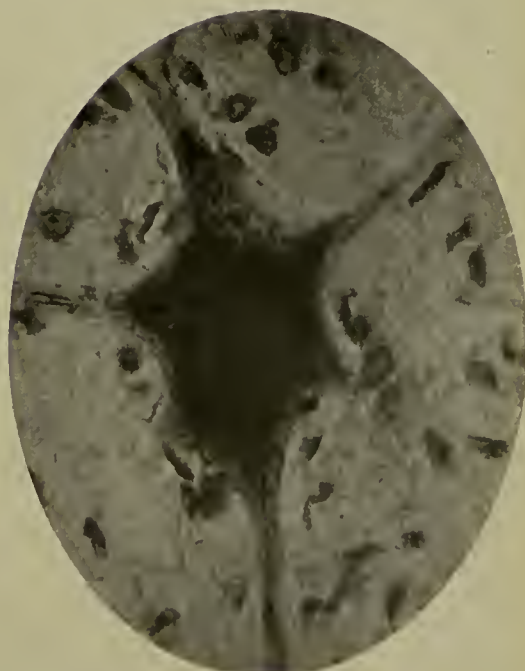


FIG. 4.



FIG. 1.

Photograph of an advanced case of Sleeping Sickness in a native, Mganda—"Dreya." An exposure of $\frac{1}{100}$ sec. with a "focal-plane" shutter was used, and even then it was found necessary to hold the head on account of the fine tremor present. Taken by Mr. R. J. Stordy.

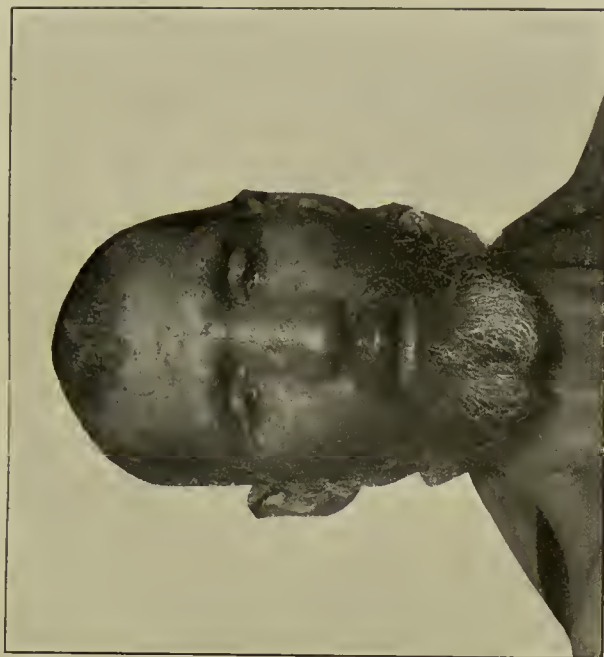


FIG. 2.

Photograph of a Persian suffering from Sleeping Sickness. Taken by Mr. R. J. Stordy, Government Veterinary Officer, Uganda and East Africa Protectorates. An exposure of $\frac{1}{100}$ sec. with a "focal-plane" shutter was used.

I am indebted to Dr. Nabarro for these two photographs, which exhibit in a striking manner the characteristic lethargic appearance which may be correlated with the advanced chronic interstitial meningeal and perrascular inflammation of the lymphatic system of the brain found in these two cases.

REPORTS

OF THE

SLEEPING SICKNESS COMMISSION

OF THE

ROYAL SOCIETY.

No. VIII.

16. Continuation Report on Sleeping Sickness in Uganda. By Lieutenant A. C. H. Gray and the late Lieutenant F. M. G. Tulloch. (With 1 plate.)
17. Report on Experiments to ascertain the ability of the Tsetse Flies to convey Trypanosoma gambiense. By P. H. Ross.
18. Report on Sleeping Sickness in Unyoro and Nile Valley. By Dr. A. Hodges. (With maps.)
19. Account of a Tour, by Mr. A. G. Speke and Dr. E. B. Adams, in Northern Unyoro and on the Victoria Nile. By Dr. E. B. Adams.
20. Report on the Anatomy of the Tsetse Fly. By Professor E. A. Minchin.
21. Glossina Palpalis in its relation to Trypanosoma gambiense and other Trypanosomes. By Professor E. A. Minchin, Lieutenant A. C. H. Gray, and the late Lieutenant F. M. G. Tulloch (with 3 plates).
22. On the Occurrence of Encystation in Trypanosoma grayi, Novy, with Remarks on the Method of Infection in Trypanosomes generally. By E. A. Minchin, M.A.

LONDON:

PRINTED FOR HIS MAJESTY'S STATIONERY OFFICE.
By DARLING & SON, LTD., 34-40, BACON STREET, E.

And to be purchased, either directly or through any Bookseller, from
WYMAN AND SONS, LTD., FETTER LANE, E.C.,
or OLIVER & BOYD, EDINBURGH;
or E. PONSONBY, 116, GRAFTON STREET, DUBLIN.

FEBRUARY, 1907.

Price Two Shillings and Sixpence.



REPORTS
OF THE
SLEEPING SICKNESS COMMISSION
OF THE
ROYAL SOCIETY.

No. VIII.

LONDON:
PRINTED FOR HIS MAJESTY'S STATIONERY OFFICE,
By DARLING & SON, LTD., 34-40, BACON STREET, E.
And to be purchased, either directly or through any Bookseller, from
WYMAN AND SONS, LTD., FETTER LANE, E.C.,
or OLIVER & BOYD, EDINBURGH;
or E. PONSONBY, 116, GRAFTON STREET, DUBLIN.

FEBRUARY, 1907.

Price Two Shillings and Sixpence.

CONTENTS.

	PAGE.
16. Continuation Report on Sleeping Sickness in Uganda. By Lieutenant A. C. H. Gray and the late Lieutenant F. M. G. Tulloch (with 1 plate)	3
17. Report on Experiments to ascertain the Ability of the Tsetse Flies to convey Trypanosoma gambiense. By P. H. Ross ...	80
18. Report on Sleeping Sickness in Unyoro and Nile Valley. By Dr. A. Hodges (with maps) ...	86
19. Account of a Tour, by Mr. A. G. Speke and Dr. E. B. Adams, in Northern Unyoro and on the Victoria Nile. By Dr. E. B. Adams ...	100
20. Report on the Anatomy of the Tsetse Fly. By Professor E. A. Minchin	106
21. Glossina Palpalis in its relation to Trypanosoma gambiense and other Trypanosomes. By Professor E. A. Minchin, Lieutenant A. C. H. Gray, and the late Lieutenant F. M. G. Tulloch (with 3 plates)	122
22. On the Occurrence of Encystation in Trypanosoma grayi, Novy, with Remarks on the Method of Infection in Trypanosomes generally. By E. A. Minchin, M.A.	137

16. CONTINUATION REPORT ON SLEEPING SICKNESS IN UGANDA.

BY LIEUTENANT A. C. H. GRAY, R.A.M.C., AND THE LATE
LIEUTENANT F. M. G. TULLOCH, R.A.M.C. (SLEEPING
SICKNESS COMMISSION).

CONTENTS.

	PAGE.
Introductory ...	5
PART I.	
The lymphatic glands in Sleeping Sickness ...	7
Hints on gland puncture ...	8
PART II.	
The cerebro-spinal fluid in Sleeping Sickness ...	9
A table of 143 lumbar punctures performed at early and late stages of this disease ...	11
PART III.	
Post-mortem examinations on cases of Sleeping Sickness ...	16
Table showing the presence of trypanosomes in the above ...	18
PART IV.	
Trypanosoma fever and its relation to Sleeping Sickness ...	18
Table showing the fate of 13 individuals in whom trypanosomes were first found in June, 1903 ...	19
Tabula ...	19
Jordien Murjan ...	21
Kumsarsabba ...	24
Mundu ...	26
Tenwa ...	28
Manawa ...	29
750 Wt 15846 2/07 D & S 32 26089	A 2

PART V.

	PAGE.
Treatment of Patients—	
Arsenic	30
Tragaroth	37
Treatment of Animals—	
Arsenic	43
Tragaroth	52

PART VI.

On the identity of the trypanosome of Sleeping Sickness with Trypanosoma gambiense	53
Tables of inoculation experiments with white rats	56
Chimpanzee inoculated with Trypanosoma gambiense	63

PART VII.

Trypanosomes in the blood of native dogs in Uganda	64
On the identity of this trypanosome with Trypanosoma gambiense ...	66

PART VIII.

The "Jinja" cattle Trypanosoma	71
Inoculation experiments on—	
White rats	73
Guinea-pigs	74
Monkeys	74
Treatment of infected animals with arsenic and trypanroth	75

INTRODUCTION.

AFTER the departure of Captain E. D. W. Greig for England on November 15, 1904, the work of the Commission at Entebbe was carried on by Lieutenant A. C. H. Gray, R.A.M.C., until he was joined on January 10, 1905, by Lieutenant F. M. G. Tulloch, R.A.M.C. The strength of the Commission was subsequently increased by the addition, for a limited period, of Professor E. A. Minchin, of University College, who reached Entebbe on April 3, 1905. The work of this observer on the relation of the Tsetse fly and *Trypanosoma gambiense*, together with some further notes by us on the trypanosomes found in freshly caught tsetse flies, will form the subject of a separate Report. Professor Minchin, having completed the task assigned to him, left for England on December 6, 1905, while Messrs. Gray and Tulloch remained to continue the work of investigation. It was arranged early in March, 1906, that Lieutenant Gray should return to England to collaborate with Professor Minchin in his Report. Unfortunately it was found on the 12th of that month that Lieutenant Tulloch was suffering from fever and his blood was found to contain *Trypanosoma gambiense*. How this disastrous result was brought about is uncertain. It may have been that he infected himself on March 2 in performing a *post-mortem* examination on a rat which died with its blood swarming with this trypanosome, but as he had suffered on at least two previous occasions from indefinite fever, it is more probable that he had been infected for some considerable time. This brought the work of the two officers to a tragical conclusion. Lieutenant Tulloch was invalided home, and he and Lieutenant Gray left Entebbe for England on April 3 last.

At this stage of the investigation it is not possible to bring forward many altogether new facts in relation to sleeping sickness. Certain lines of work were suggested to the members of the Commission by the Tropical Diseases Committee of the Royal Society in April last which they have tried to follow out. Additional evidence is now brought forward in favour of the correctness of the conclusions arrived at in the last Report, together with a few fresh facts, which may be summarized as follows :—

- (1.) That trypanosomes are constantly present in the lymphatic glands of early and late cases of trypanosome infection, and can be found there on any day of the disease.
- (2.) That the subsequent incidence of sleeping sickness is much higher among natives in whom gland-enlargement has been previously noted than among those in whom no such condition has been found.

- (3.) That trypanosomes are not present in the cerebro-spinal fluid of very early cases of trypanosome infection, but that these parasites can always be found there in late stages of the disease.
- (4.) That sleeping sickness is the last stage of trypanosome infection and is always fatal. The after-history of cases noted some three years ago by previous members of this Commission has been carefully followed out and only one man now certainly remains alive.
- (5.) That trypanosomes can nearly always be found on post-mortem examination of cases of sleeping sickness, provided that such examination be made within a few hours of death.
- (6.) That the treatment of trypanosome infection with drugs does not hold out much hope of success even in early cases.
- (7.) That chimpanzees are readily infected with the trypanosome of sleeping sickness, that gland enlargement soon follows in them, and that parasites are numerous in their enlarged glands. The one experimental chimpanzee in the hands of the members of the Commission closely resembled a man in the early stage of trypanosome infection, but unfortunately he soon died from captivity.
- (8.) That there is but one human trypanosome in Uganda and that it is identical with *Trypanosoma gambiense*.
- (9.) That native dogs in an area of sleeping sickness have been found by the Commission to be infected with a trypanosome, and that this trypanosome is most probably identical with the trypanosome of sleeping sickness.
- (10.) That the drug treatment of artificially infected animals with almost poisonous doses has proved of little value.
- (11.) That the trypanosome of the "Jinja cattle disease," if not *Trypanosoma Brucei*, is a very closely allied species; and that drug-treatment in the case of this trypanosome has proved successful with one monkey only, inoculated with this disease.

Sleeping sickness in Uganda seems to be surely spreading still further afield. The outbreak at Bugungu on Lake Albert, referred to in the previous Report, has assumed more serious proportions. It would seem from information sent to the Commission by Dr. Ashton Bond that the Toro district has also become infected. *Glossina palpalis* has been brought to Messrs. Gray and Tulloch from such a southerly point as the shore of Lake Tanganyika.

An extensive scheme for accurately mapping out the areas infested with Tsetse fly and with sleeping sickness in Uganda is now on foot under the direction of Dr. A. Hodges.

The present members of the Commission wish, in the first place, to thank Colonel D. Bruce, C.B., F.R.S., for his constant encouragement and advice in the work, and for his kindness in correcting the proofs of this Report; Professor E. A. Minchin for his numerous and valuable suggestions on the subjects of investigation, and Captain E. D. W. Greig, I.M.S., who has been in constant communication with the Commission since his departure. Their sincere thanks are also due to Colonel Hayes-Sadler, C.B., His Majesty's Commissioner and Consul-General, Uganda, for his invariable kindness in providing facilities for the work; to Mr. George Wilson, C.B., His Majesty's Acting Commissioner for Uganda, for his helpfulness in procuring a chimpanzee for experiment and for the many other ways in which he has shown his interest in the progress of the researches; to Lieut.-Col. J. Will, P.M.O.; to Dr. R. U. Moffat, C.M.G., for valuable assistance and advice; to several other helpers who have kindly provided us with blood films from various wild animals; and to the Bishops and Missionaries of the various churches who have greatly furthered the investigation by sending cases of sleeping sickness, and by observing natives under their control.*

I.—*The lymphatic glands in Sleeping Sickness.—Gland punctures.*

The earliest descriptions of sleeping sickness mention enlargement of the lymphatic glands as a prominent and early feature of the disease. The natives of Uganda look on this gland enlargement as an early sign of infection, and have even advocated the removal of the enlarged glands as a means of cure. Slight enlargement of the superficial lymphatic glands becomes apparent probably within one or two months of infection and persists all through the course of the disease. It is often, however, less marked in those late cases, where life will last only a few weeks longer, than in the earlier stages where the other symptoms are but slight. All the glands of the body are more or less involved and the superficial glands of the neck and axilla show this enlargement quite early in the disease. The typical enlarged gland is smooth, separate, moveable and soft, about five-eighths

* Since these lines were written Lieutenant Tulloch has succumbed to his illness (20th June, 1906). A career of great promise has thus been sadly and prematurely closed. The Tropical Diseases Committee of the Royal Society takes this opportunity of expressing its great sorrow at the loss of one to whom it owes a tribute of sincere gratitude for the enthusiasm and ability which he devoted to the difficult and dangerous task entrusted to him. A martyr to science, he passed away before the last records of his labours had been given to the world. These records of work carried on jointly by him and Lieutenant Gray have been finally arranged and revised by the latter and are given in the present Report.—[Sec. R.S.]

by three-eighths of an inch in size, and with the consistency of a ripe damson, giving the impression, on palpation, that hard pressure would cause it to burst. This gland enlargement is rarely visible to the eye alone, except in emaciated individuals.

In our examination of persons supposed to be infected with Trypanosomes we have regularly employed the method of gland puncture first described in the "Proceedings of the Royal Society" for May 1904 (Greig & Gray). We have used this method alike on natives of Africa, on Indians and on Europeans, and have found it uniformly successful and practically painless.

When dealing with the timid native of Africa, several small points are worth attending to and help towards a successful examination. The posterior cervical glands are by far the most suitable for puncture, because they are superficial, easily handled, and practically always enlarged, while at the same time the operation cannot be seen by the patient. The needle of the hypodermic syringe used should be as fine and as sharp as possible, and the piston of the syringe should give good suction when drawn out of the barrel. The instrument should be carefully kept out of sight of the patient. A suitable enlarged gland is then found and picked up between the finger and thumb, the patient is then warned that he will only feel a sharp prick, and the needle (with syringe attached) is at once sharply pushed through the skin and well into the middle of the gland substance. The point of the hypodermic needle is now gently moved about in the gland substance and an assistant asked to slowly draw out the piston of the syringe and to keep it drawn out. The barrel of the syringe is then detached from the needle, leaving the needle alone sticking into the gland. The needle with its contained drop of juice is then carefully removed from the gland; the barrel of the syringe is again attached and the drop of juice is at once blown out into and mixed with a minute drop of normal citrate solution kept ready to hand on a glass slide.

If the needle and syringe are both withdrawn together from the gland, the drop of gland-juice is usually found immediately to run up into the barrel of the syringe instead of staying in the needle, and can hardly be got out again for examination; but if the simple precaution here noted is taken no such difficulty arises. Another small precaution, which we have found useful in very hot weather, is to have the hypodermic needle (not barrel of syringe) full of normal citrate solution at the time of puncture, thus preventing any possibility of the drop of gland-juice drying up before it is blown out on to the slide for examination. By this method of gland-puncture we have over and over again at once found trypanosomes in persons whose blood and cerebro-spinal fluid had proved negative after a prolonged search.

We wish to lay special stress on the fact that trypanosomes are practically always present in the lymphatic glands of an infected person, and can be found there on any day and at any stage of the disease. It is true that in some cases the gland-juice

shows more parasites at one time than at another, but trypanosomes can nearly always be found in a fresh specimen of the juice without any difficulty. For confirmation of this statement, we would refer the reader to the table of gland, blood and spinal fluid examinations on page 11. MB

Within 24 hours of death we have often noticed that living trypanosomes could not be found in the gland-juice, and it has been quite exceptional to find parasites in the glands at a *post-mortem* examination. We consider that this fact is due to a terminal bacterial invasion causing the death of the trypanosomes.

In June, 1904, 64 apparently healthy natives who lived on Sesse Island were examined by the Rev. H. T. C. Weatherhead. Each individual was carefully examined for gland enlargement, and full particulars for future identification were recorded. It was found at this time that 30 out of these 64 men showed a definite enlargement of their cervical lymphatic glands.

In July, 1905, just a year later, Mr. Weatherhead again visited this island and examined the same individuals, or such of them as were still alive. He found that nine of these 64 men had died of or were in the last stages of sleeping sickness, and that all except one of these nine men had been noted by him as showing marked gland-enlargement the year previously although otherwise seeming perfectly healthy. These results show then that of a given number of natives who all show enlargement of their lymphatic glands but seem otherwise healthy, one-third will be found to have died from sleeping sickness within a year from such examination. The very fact of enlargement of the glands of the neck, presenting the characters mentioned above, may thus be taken to be of itself almost sufficient proof of trypanosome infection if it occurs in inhabitants of a sleeping sickness area.

II.—*The Cerebro-spinal Fluid in Sleeping Sickness. An account of 143 lumbar punctures performed at early and late stages of this disease.*

Since November 1904, 40 patients have been admitted to our hospital as either early or late cases of sleeping sickness. 32 of these patients are dead, all but one of them having undoubtedly died from sleeping sickness as proved by the clinical course of the disease and by *post-mortem* examination.* Trypanosomes have been found in the cerebro-spinal fluid of 30 out of these 31 fatal cases of sleeping sickness at some time or other before death. The one case in which trypanosomes were not found was only examined a few hours before death.

* The one case (Rehani, No. 36) died from sarcoma of the cervical glands with secondary deposits in the internal organs. Trypanosomes were also present in the blood of this man; but a microscopical examination of his brain after death showed no small-celled infiltration so typical of sleeping sickness, nor were trypanosomes found in his cerebro-spinal fluid during life, so that no doubt in his case the trypanosome infection was quite recent.

We have omitted from the following list any lumbar punctures performed by us in which the resulting spinal fluid was found to be contaminated with blood to any appreciable extent, if trypanosomes were also found to be present in a blood-film taken at the time of the operation. All these cases showed marked lethargy which deepened into coma as death approached. In nearly every case the temperature was sub-normal for several days before death.

On these 31 fatal cases of sleeping sickness, 104 lumbar punctures have been performed at varying periods before death, with the following results :—

TABLE I.

The examination of the cerebro-spinal fluid of 31 fatal cases of Sleeping Sickness for <i>Trypanosoma gambiense</i> .	Trypanosomes present in	Trypanosomes absent in
Of 43 examinations made more than 100 days before death.	18	25
Of 61 examinations made within 100 days of death.	58	

In these last three fatal cases in which trypanosomes were not found, the lumbar punctures were performed within 24 hours of death.

On the remaining 14 cases who are still alive, 39 lumbar punctures have been performed, with the following results :—

TABLE II.

The examination of the cerebro-spinal fluid of 14 cases of Sleeping Sickness, who are still alive, for <i>Trypanosoma gambiense</i> .	Trypanosomes present in	Trypanosomes absent in
Of 6 examinations made on five very early cases.	0	6
Of 25 examinations made on four intermediate cases.	15	10
Of 8 examinations made on five late cases ...	8	0

These observations entirely corroborate the original statement made by Col. Bruce, that “*the cerebro-spinal fluid of every case of sleeping sickness contains trypanosomes during life.*”

We have had the opportunity of examining the cerebro-spinal fluid in a few early cases wherein no symptoms had been detected other than occasional fever and the presence of trypanosomes in their blood and lymphatic glands. In these cases the cerebro-spinal fluid has been found by us to be perfectly normal ; containing no trypanosomes, and with only the slightest trace of cellular deposit after centrifuging. We may say then,

from the observations we have had an opportunity of making, that *the cerebro-spinal fluid of early cases of trypanosome infection does not contain trypanosomes.*

When we come to consider the cases between these two extremes, that is to say, the cases between 100 and 300 days of death, of 30 lumbar punctures actually performed by us, 22 have been positive and eight negative.

We give the following table, which shows the date and the number of days before death of any given lumbar puncture, and also the state of the blood, as shown by a large blood film, and gland juice at the time of the operation. In every case 20 cubic centimetres of cerebro-spinal fluid were drawn off, centrifuged at once for five minutes, and the whole deposit was examined fresh. As above stated, in early cases of trypanosome infection we have always found that the white cell-elements are exceedingly scanty, appearing as only a slight film at the bottom of the test tube after centrifuging. We have likewise observed the presence of trypanosomes in the cerebro-spinal fluid to be accompanied by some increase in the number of white cells, and that as death draws near the number of white cells increases. We have noted in several cases within a day or two of death that trypanosomes could not be found in the cerebro-spinal fluid which on former examinations had constantly shown parasites, but that the cellular deposit was as large or even larger than before. Probably the presence of large numbers of diplococci may be responsible for the disappearance of the trypanosomes.

TABLE III.

Showing the Result of Examinations of the Cerebro-spinal fluid, Blood and Gland-juice of 46 cases of Sleeping Sickness for Trypanosoma gambiense :—

Name.	Date.	Number of days before death.	Trypanosomes		Cerebro-spinal fluid.	
			In Blood.	In Glands.	Trypanosomes.	Leucocytes.
Timitao ...	12.9.04	74	—	...	+	Slight incr.
M. 25 yrs.	17.11.04	8	—	+	+	Incr.
(1)	25.11.04	Autopsy	—	—	—	"
Abyabu ...	15.8.04	133	+	+	+	Slight incr.
M. 20 yrs.	23.9.04	94	+	+	+	"
(2)	21.11.04	35	—	+	+	Incr.
	20.12.04	6	—	+	+	Large incr.
	26.12.04	Autopsy	—	—	+	"
Badingo ...	3.10.04	86	—	+	+	Incr.
M. 20 yrs.	25.11.04	33	—	+	+	"
(3)	26.12.04	2	+	+	+	Large incr.
	28.12.04	Autopsy	—	—	+	"

Name.	Date.	Number of days before death.	Trypanosomes		Cerebro-spinal fluid.	
			In Blood.	In Glands.	Trypanosomes.	Leucocytes.
Zenabu ...	11.1.05	81	—	+	+	Slight incr.
F. 19 yrs.	1.3.05	32	—	+	+	"
(4)	30.3.05	3	+	+	+	Incr.
	2.4.05	Autopsy	+	+	+	"
Kaparaga ...	4.1.05	25	—	+	+	"
M. 28 yrs.	27.1.05	2	—	+	+	"
(5)	29.1.05	Autopsy	—	—	—	"
Suddwaka ...	21.1.05	52	—	+	+	"
M. 22 yrs.	6.3.05	8	—	+	+	Large incr.
(6)	14.3.05	Autopsy	—	—	+	"
Keranya ...	17.2.05	23	—	+	+	Slight incr.
M. 29 yrs.	8.3.05	4	—	+	+	Great incr.
(7)	12.3.05	Autopsy	—	—	—	"
Tumbo ...	6.3.05	48	+	+	+	Slight incr.
M. 10 yrs.	19.4.05	4	—	+	+	Incr.
(8)	22.4.05	Autopsy	—	—	+	Great incr.
Monica ...	20.2.05	29	—	+	+	Incr.
F. 12 yrs.	7.3.05	14	—	+	+	"
(9)	21.3.05	Autopsy	+	+	+	"
Jabolas ...	11.3.05	13	+	+	+	"
M. 9 yrs.	24.3.05	Autopsy	—	—	+	"
(10)						
Kenduga ...	20.3.05	34	+	+	+	"
M. 24 yrs.	14.4.05	9	—	+	+	"
(11)	23.4.05	Autopsy	—	...	+	Great incr.
Zerimenya ...	22.4.05	23	—	+	+	Incr.
M. 28 yrs.	12.5.05	3	—	+	+	"
(12)	15.5.05	Autopsy	+	—	+	"
Almasi ...	6.12.04	1	—	+	—	Great incr.
M. 32 yrs.	7.12.04	Autopsy	—	—	—	"
(13)						
Maharabu ...	22.12.04	17	—	+	+	Great incr.
Swahili.	9.1.05	Autopsy	—	—	—	"
M. 26 yrs.						
(14)						
Zake ...	11.5.05	6	+	+	+	Incr.
M. 23 yrs.	17.5.05	Autopsy	—	—	+	Great incr.
(15)						
Vule ...	9.3.05	11	—	+	+	"
M. 21 yrs.	20.3.05	Autopsy	—	—	—	"
(16)						

Name.	Date.	Number of days before death.	Trypanosomes		Cerebro-spinal fluid.	
			In Blood.	In Glands.	Trypanosomes.	Leucocytes.
Wasaneri ...	18.3.05	81	—	+	+	...
M. 26 yrs.	7.5.05	30	—	+	+	Incr.
(17)	31.5.05	6	—	+	+	Great incr.
	2.6.05	4	—	—	—	"
	6.6.05	Autopsy	—	—	—	"
Zakibu ...	9.5.05	...	—	+	+	...
M. 24 yrs.	9.6.05	...	+	+	+	Incr.
(18)	11.7.05	...	—	+	+	"
	8.8.05	Still alive.	—	—	+	"
Sururu	1.7.05	1	—	+	+	Great incr.
Morjan.	1.8.05	Autopsy	—	—	—	"
Nubian. M.						
(19)						
Vikitdyeya ...	8.5.05	20	—	+	+	Incr.
F. 23 yrs.	23.5.05	5	—	+	+	"
(20)	28.5.05	Autopsy	—	—	+	"
Thomasadi ...	26.5.05	30	—	+	+	"
M. 26 yrs.	25.6.05	Autopsy	—	—	+	"
(21)						
Busaja ...	16.1.05	165	—	+	—	Very few.
M. 19 yrs.	8.3.05	114	+	+	—	Slight.
(22)	6.5.05	55	—	+	+	"
	15.6.05	15	—	+	+	"
	29.6.05	1	—	+	+	Slight incr.
	30.6.05	Autopsy	+	+	+	"
Jabu Brahim	12.5.05	60	+	+	+	Incr.
Swahili.	2.6.05	32	+	+	+	"
M. 26 yrs.	4.7.05	Autopsy	—	—	+	"
(23)						
Hamesi ...	26.11.04	219	+	+	—	Very few.
M. 28 yrs.	28.12.04	187	+	+	+	"
(24)	24.2.05	153	+	+	+	Slight incr.
	13.5.05	61	—	+	+	Incr.
	17.6.05	18	+	+	+	Few.
	3.7.05	2	—	+	+	"
	5.7.05	Autopsy	—	—	+	Many.
Punda Mulia	14.7.05	72	—	+	+	Incr.
(25)	12.8.05	36	—	+	+	Large incr.
	17.9.05	Autopsy	—	—	—	"
Babula ...	23.11.05	1	+	+	+	Great incr.
(26)	24.11.05	Autopsy	—	—	—	"
Jumma ...	23.11.05	15	—	+	+	Incr.
(27)	7.12.05	1	—	+	—	"
	8.12.05	Autopsy	—	—	—	"

Name.	Date.	Number of days before death.	Trypanosomes		Cerebro-spinal fluid.	
			In Blood.	In Glands.	Trypanosomes.	Leucocytes.
Moanica ...	7.12.05	21	—	+	+	Incr.
M. 28 yrs. (28)	28.12.05	Autopsy	—	—	+	Great incr.
Upungu ...	8.5.05	...	—	+	+	Very scanty.
M. 20 yrs. (29)	8.6.05	...	—	+	+	"
	10.7.05	Still alive.	—	+	+	"
Sabakaki ...	25.5.05	...	+	+	+	Scanty
(30)	10.6.05	Still alive.	—	+	+	"
Manawa ...	9.6.04	...	—	+	—	Very few.
M. 25 yrs (31)	10.5.05	...	—	—	—	"
	16.6.05	...	—	—	+	...
	25.7.05	...	—	—	+	Very few.
	18.8.05	...	—	...	+	"
	23.9.05	...	—	...	—	"
	28.10.05	...	—	...	—	"
	7.12.05	...	—	—	—	"
	7.1.06	Still alive.	—	—	+	Slight incr.
Jordien	31.3.03	838	+	...	—	...
Murjan.	17.4.03	821	—	...
Nubian. M. (32)	1.5.03	807	+	...	—	...
	11.5.03	796	+	...	—	...
	25.5.03	782	+	...	—	...
	9.6.03	767	+	...	—	...
	23.6.03	753	+	...	—	Very few.
	22.7.03	724	+	...	+	...
	18.8.03	697	+	...	+	...
	21.9.03	663	+	...	—	...
	9.10.03	614	+	...	—	...
	26.12.03	566	+	...	+	...
	1.2.04	530	—	...
	21.3.04	461	+	+	—	...
	7.6.04	383	+	+	+	Very few.
	18.7.04	342	—	+	+	"
	25.8.04	304	+	+	+	"
	2.10.04	266	+	+	+	...
	13.12.04	194	+	+	+	Incr.
	3.1.05	173	+	+	+	"
	8.4.05	78	...	+	+	"
	30.5.05	26	+	+	+	Great incr.
	26.6.05	Autopsy	—	—	+	"
Sengoma ...	9.5.05	170	+	+	+	Few.
M. 23 yrs. (33)	7.6.05	141	—	+	+	"
	7.7.05	111	—	+	+	Incr.
	4.8.05	83	—	+	+	"
	14.9.05	42	+	+	+	Great incr.
	25.10.05	1	—	+	+	"
	26 10.05	Autopsy	—	—	+	"

Name.	Date.	Number of days before death.	Trypanosomes		Cerebro-spinal fluid.	
			In Blood.	In Glands.	Trypanosomes.	Leucocytes.
Mondu ... M. 25 yrs. (34)	9.7.04	533	+	+	—	Very few.
	4.11.04	413	—	+	—	"
	11.5.05	231	—	...	+	"
	14.6.05	191	—	...	+	Slight incr.
	11.7.05	165	—	...	+	"
	17.8.05	127	—	...	+	Incr.
	23.9.05	90	—	...	+	"
	28.10.05	55	—	...	+	"
	6.12.05	16	+	...	+	Great incr.
	22.12.05	Autopsy	—	...	+	"
Tenwa ... M. 25 yrs. (35)	7.6.04	...	—	+	—	...
	4.11.04	...	—	—	—	...
	10.5.05	...	—	...	+	Very few.
	10.7.05	...	—	...	—	Incr.
	18.8.05	...	—	...	+	"
	23.9.05	...	—	—	+	"
	28.10.05	...	—	—	—	Very slight.
	6.12.05	...	—	...	—	Slight incr.
	5.1.06	Alive	—	—	+	"
Rehani ... M. 35 yrs. (36)	10.1.06	1	+	—	—	Very scanty.
	11.1.06	Autopsy	+	—	—	Scanty.
Retero ... M. 18 yrs. (37)	6.12.05	...	—	+	+	Great incr.
	5.1.06	Still alive.	—	+	+	"
Mataisa ... (38)	4.1.06	"	—	+	+	Very few.
Kcosi ... (39)	4.1.06	"	—	+	+	Large incr
Lufumina ... (40)	6.12.05	...	—	+	+	Incr.
	15.1.06	Still alive.	—	+	+	"
Zekya ... (41)	10.1.06	...	+	+	—	Very few.
	15.1.06	Still alive.	—	+	—	"
Tabula ... M. (42)	15.4.03	777	+	...	—	...
	6.5.03	756	—	...
	25.6.03	706	—	...	—	...
	22.8.03	648	—	...	—	...
	5.1.04	523	—	...
	27.6.04	360	—	+	—	...
	5.12.04	189	—	+	—	...
	14.2.05	118	—	+	+	Incr.
	13.5.05	30	—	+	+	"

Name.	Date.	Number of days before death.	Trypanosomes		Cerebro-spinal fluid.	
			In Blood.	In Glands.	Trypanosomes.	Leucocytes.
Halone ...	18.1.06	Still alive.	—	+	—	Very few.
Mr. Z. ...	26.5.05	"	+	+	—	"
Indian L.S. ...	19.1.06	"	+	+	—	"
Yusufu M. 16 yrs.	8.7.05	"	+	+	—	"

III.—*An analysis of 32 post-mortem examinations performed on cases of Sleeping Sickness.*

Out of a total of 32 *post-mortem* examinations made on cases of sleeping sickness since November, 1904, actively motile trypanosomes have been found in the cerebro-spinal fluid of 20. In 24 cases the examination was made within five hours after death, and in as many as 19 of these cases motile trypanosomes could be found in the cerebro-spinal fluid.

An analysis of these 32 *post-mortem* examinations shows—

Trypanosomes present in a blood film	5 times.
" " the brain	11 "
" " cerebro-spinal fluid	20 "
" " lymphatic glands	3 "
Diplo-cocci were present in the brain	22 "
" " " cerebro-spinal fluid	28 "
" " " spleen	27 "
Superficial ulceration of the stomach was found to be present	23 "
Complications sufficient in themselves to be a cause of death	7 "

These complications consisted of lobar pneumonia 2; purulent meningitis, 2; ulcerative endocarditis, 1; general acute pleurisy, 1; sarcoma of cervical glands, with deposits in liver and spleen, 1.

In the majority of cases the body showed marked emaciation, and bed-sores were often present.

The skin was generally very dry and harsh, old scabs and scratch marks being very common. The feet and sometimes the hands were frequently infested with "chiggers." The lymphatic glands, both superficial and deep, were always enlarged, this enlargement being especially noticeable in the deep cervical and axillary groups. In these regions the glands presented their characteristic soft, moveable character, were enlarged to some four or five times the normal size and were often hæmorrhagic

on section. The glands of the groin were always enlarged but were generally hard or else showed points of suppuration due no doubt to the septic condition of the feet. Localised œdema was seen occasionally, two cases showing marked œdema of the feet. Œdema of the eyelids was a prominent feature in three cases. The pupils were never noticed to be unequal. The dura mater was often thickened and in places adherent to either the bone or pia arachnoid. The cerebro-spinal fluid was nearly always increased in amount and very cellular. The blood vessels on the surface of the brain were generally engorged. The leptomeninges often showed patches of localised thickening and opacity, especially at the base of the brain. The brain substance appeared normal. The lungs were generally very œdematous and congested; old pleurisy was often seen. Minute petechial hæmorrhages were seen under the pleura on the surface of both lungs on several occasions. The heart was as a rule pale and flabby with its cavities somewhat dilated. The liver very often showed a "nutmeg" appearance on section. The spleen was constantly considerably enlarged and generally seemed congested. The mucous membrane of the stomach, as mentioned above, showed a varying amount of superficial ulceration in as many as 23 cases. (*See Report VI., of Sleeping Sickness Commission of Royal Society, page 266.*) We have not seen this condition of the stomach, so far, in the few *post-mortem* examinations we have witnessed, on natives who have died from diseases other than sleeping sickness.

A well marked small-celled infiltration around the blood vessels was seen in sections of those brains which were microscopically examined,—13 in all. Sections of these brains were stained by Leishman's method for demonstrating chromatin in sections, in the hope that trypanosomes would be observed in the brain substance. On one occasion only were we able to see trypanosomes in this way and then only in very scanty numbers. However, in smears of brain, trypanosomes have been seen in 11 cases, more often in smears from the brain surface than from the deeper parts. In examining these brains for trypanosomes our usual method has been to make emulsions of the various parts of the brain in normal citrate solution with the help of a pestle and mortar, to then centrifuge these emulsions and to examine drops of the resulting deposits fresh. If trypanosomes were found in any of these deposits, a drop of fresh blood serum was added, well mixed with the deposit and smeared out for staining.

Actively motile trypanosomes can nearly always be found somewhere in the body of a patient who has died of sleeping sickness, provided that the examination be made within an hour or two after death. In by far the greater number of cases these trypanosomes will be most easily found in either the cerebro-spinal fluid or emulsions of the brain substance. In our experience we have but rarely found parasites in the blood after

death, and still more rarely in the lymphatic glands. In one case trypanosomes were numerous in the pericardial fluid as well as in the blood and cerebro-spinal fluid after death.

TABLE IV.

Showing the Results of the Post-mortem Examination of the Blood, Brain, and Cerebro-spinal Fluid of 32 cases of Sleeping Sickness for Trypanosoma gambiense.

Name	No. of Hours after Death.	Trypanosomes found in			
		Blood.	Brain.		Cerebro-spinal Fluid.
			Cortex.	Centre.	
1. Timateo	14	—	—	—	—
2. Abyabu	1	—	—	—	+
3. Badingo	1	+
4. Zenabu	3	+	—	—	+
5. Kaparaga	2	—	—
6. Suddwaka	1	—	+
7. Keranya	1 $\frac{1}{2}$	—	—
8. Tumbo	$\frac{1}{2}$	—	+	—	+
9. Monica	$\frac{1}{2}$	+	—	...	+
10. Jabolas	3	—	—	—	+
11. Kenduga	$\frac{1}{2}$	—	+	—	+
12. Zerimenya	$\frac{1}{2}$	+	+	—	+
13. Almasi	10	—	—	—	—
14. Maharubu	12	—	—
15. Zake	3	—	+	—	+
16. Vule	1 $\frac{1}{4}$	—	—	—	—
17. Wasaneri	1	—	—	...	—
18. Sururu Morjan	12	—	—	+	—
19. Vikitdyeya	1	—	+	—	+
20. Thomasidi	4 $\frac{1}{2}$	—	+	—	+
21. Busaja	$\frac{1}{2}$	+	+	—	+
22. Jabu	$\frac{1}{2}$	—	—	—	+
23. Hamesi	9 $\frac{1}{2}$	—	+	—	+
24. Pundamulia	10	—	—	—	—
25. Babula	9	—	—	—	—
26. Juma	10	—	—	—	—
27. Moanica	3 $\frac{1}{2}$	—	—	+	+
28. Jordien Murjan	1 $\frac{1}{2}$	—	—	—	+
29. Sengoma	2 $\frac{1}{2}$	—	—	—	+
30. Mondu	$\frac{1}{2}$	—	—	+	+
31. Rehani	$\frac{1}{2}$	+	—	—	—
32. Musajabura	4	—	—	—	+

IV.—*Human Trypanosomiasis and its relation to Sleeping Sickness.*

In June, 1903, Colonel Bruce and the other members of this Commission found trypanosomes in the blood of 23 persons, all but one of whom were natives of Africa. All these men then

presented the ordinary symptoms of *Trypanosoma* fever, that is to say, they suffered from irregular periods of fever, headache and malaise, their glands were enlarged and trypanosomes could be found in their blood at varying intervals. Unfortunately all traces of 10 of these individuals have been lost, but the remaining 13 have been under more or less continual observation, and their histories are very striking. At the present time (April, 1906) only one of these 13 men is alive, and he is now beginning to show symptoms of sleeping-sickness trypanosomes have been continually found either in his blood or glands from the very beginning. (*See case, Kumsarsabba, page 24.*)

Of the remaining 12 individuals, 10 have already died of sleeping sickness and two of pneumonia. The following table gives their names and the date of their death:—

TABLE V.

List of Individuals in whose blood Trypanosomes were first discovered in June, 1903, giving the date and cause of death.

Name.	Date of Death.	Cause of Death.
Mucase	Dec. 13, 1903 ...	Sleeping sickness.
Saulo	Dec. 2, 1903 ...	" "
Gabula	Jan. 1904	" "
*Karala Barigi	April 18, 1904 ...	Pneumonia.
*Bara Risgallah	May 5, 1904	" "
Kululwe	Dec., 1904	Sleeping sickness.
Buza	March 2, 1905 ...	" "
Kitungula	March, 1905	" "
Tevamukopi	April, 1905	" "
†Tabula	June 12, 1905 ...	" "
†Jordien Murjan	June 26, 1905 ...	" "
J. M. (European)	April, 1906	" "
Kumsarsabba	Alive on April 3, 1906, but is showing early symptoms of sleeping sickness.	

* For details *see* Report No. VI. of this series, page 40.

† A detailed account of these cases follows.

CASE 66. TABULA (MALE). AGE 25. TRYPANOSOMA FEVER.

District, Marine Village, Entebbe. Occupation, Marine.

April 15, 1903. Is a marine of one year's service, lives in the Marine Village where he says there are no cases of sleeping sickness. He used to live in Entebbe. He says that he has been ill for nine days and does not remember ever being ill before. He complains of slight headache. Pulse, 96; temperature, 100°; speech, quite normal; tongue moist and clean, not tremulous. There is no tremor of the fingers. Cervical lymphatic glands slightly enlarged. Enlarged glands in both groins. Trypanosomes are present in a blood film, but not in the cerebro-spinal fluid.

April 20. Temperature is normal to day, having been persistently raised for the last five days.

May 11. Discharged from hospital to-day, his temperature having remained normal.

June 4. Temperature, 100·6°. Trypanosomes not present in the blood.

August 22. Patient is at his work and complains of nothing. His gait is normal, there is no tremor. His cerebro-spinal fluid has been examined five times since April, but has never shown the presence of trypanosomes.

November 13. Patient shows no signs of sleeping sickness; he is at his work and says that he is quite well. The occipital glands are slightly enlarged and those in the anterior triangle markedly so. The axillary and femoral glands are also enlarged. The fingers seem to be slightly tremulous. There is tremor of the tongue. The gait and expression are quite normal. There is no pain. Pulse, 80. Temperature, normal.

January 5, 1904. Complains of headache and pain in the eyes. Pulse, 68. Slight tremor of tongue and hands. Glands enlarged.

March 29. He is reported to be very dull and stupid at his work. Pulse, 80. Removed an enlarged lymphatic gland from the anterior triangle of the neck. Numerous and actively motile trypanosomes are present in the gland juice. Tongue is tremulous.

June 13. Facial expression is dull. Tremor of tongue and hands. Pulse, 120. Lymphatic glands generally enlarged in all the regions. Patient would not allow any examination of his cerebro-spinal fluid. Trypanosomes present in the gland juice and in a blood film.

June 27. Patient found asleep on duty. Examined cerebro-spinal fluid, trypanosomes are absent.

December 5. He is getting distinctly drowsy. Trypanosomes absent from the cerebro-spinal fluid.

February 8, 1905. Patient shows marked signs of sleeping sickness. Tremor of tongue and fingers has increased. He is drowsy, the voice is weak and his speech slow. The gland enlargement remains as before. Temperature, 104°. Admitted into the native hospital.

February 14. Removed 20 c.c. cerebro-spinal fluid. The cellular deposit is larger than before. Trypanosomes are present in moderate numbers. The cerebro-spinal fluid is under considerable pressure. It is sterile. Trypanosomes present in the lymphatic gland juice, but are absent from a blood film. Patient says that he feels weak and drowsy. He speaks normally, but his gait is uncertain. There is no wasting; his appetite is fairly good. He complains of headache. There is marked tremor of the tongue and fingers.

February 21. Injections of perchloride of mercury started.

March 4. Patient has had daily injections of mercury, $\frac{1}{2}$ th grain, but without any marked effect. His temperature has varied between 99° and 101° every evening since admission.

May 13. Patient remains in much the same state. His temperature, though above normal, is not so high as it was. Drowsiness is increasing. Speaks in a very slow weak voice when roused. Tremor is marked. Examined the cerebro-spinal fluid; trypanosomes are present and numerous.

June 3. Patient managed to crawl out of bed yesterday and fell down, cutting his head. The fall has been followed by twitching of all the limbs and choreiform movements which came on soon after the fall and which lasted many hours afterwards.

June 7. Patient's temperature has sunk to sub-normal and he is moribund.

June 8. Patient removed from the hospital in the night by his friends. A few days later news was brought that patient was dead, but a *post-mortem* examination was not allowed.

The following table shows the presence or absence of trypanosomes in the blood, glands, and cerebro-spinal fluid :—

Date.	Parasites in Blood.			Parasites in Glands.		Parasites in Cerebro-spinal Fluid.	
	Fil.	Mal.	Tryp.	Strept.	Tryp.	Strept.	Tryp.
1903.							
April 15
" 17
May 6
" 20
June 4
" 25
Aug. 22
Sept. 25
Nov. 13
1904.							
Jan. 5
March 29
June 13
" 27
Dec. 5
1905.							
Feb. 1
" 8
" 14
May 13

This man's temperature followed the usual course. There was constant fever for seven months before death. About a fortnight before death the temperature became sub-normal.

CASE 64. JORDIEN MURJAN. MALE. AGE 36.

District, Muru. Nubian. Prisoner for last three years.

March 31, 1903. Admitted to hospital. No œdema, no noticeable swelling of glands. Tongue healthy, but shaky. No tremor of hands. Speech is normal and pulse 144.

August 18. This patient at the present date has not any marked symptoms of sleeping sickness. At the same time, there is slight general enlargement of the lymphatic glands, his expression is dull, there is some tendency to tremor of the tongue and fingers, and his pulse is rapid.

September 21. Expression is dull and heavy. Complains of no pain. Appetite good. Pulse 136. Slight tremor of tongue and fingers.

November 9. No definite signs of sleeping sickness. Pulse 120. Fine tremor of tongue.

December 26. Tremor of fingers distinct. Trypanosomes present in the cerebro-spinal fluid.

February 1, 1904. General condition as before.

March 21. A gland in left anterior triangle of neck was removed ; active trypanosomes were present in the juice.

June 7. Pulse 104. No pain. Tremor of hands and tongue present. Œdematous swellings of both legs. Cerebro-spinal fluid contains active trypanosomes ; no red cells. He is reported to be "very dull and stupid and fit for very little work."

July 18. Complains of pain in head, arms and chest, also of itching. Pulse 125. Active trypanosomes in cerebro-spinal fluid ; no red cells in the deposit.

August 25. Complains of no pain. Pulse is 120. Œdema of right foot. Trypanosomes present in cerebro-spinal fluid ; no red cells.

October 2. Tremor of hand ; no pain. Slight œdematous swelling of left foot. Trypanosomes in cerebro-spinal fluid ; no red cells in deposit.

December 13. Pulse 110. Patient seems in just the same state. Œdema of both feet. Trypanosomes in cerebro-spinal fluid.

February 8, 1905. Pulse 100. Slight tremor of tongue and lips. Complains of nothing. Is reported to be very dirty and to do no work at all.

April 8. Face very dull looking and expressionless. Heavy tired look about the eyes. Complains of nothing, maintains a very sullen attitude. Gland enlargement quite marked on both sides of neck and in both axillæ. Glands soft and moveable. Skin very dry and harsh. Œdema of both feet and around both eyes. He is able to walk a short distance without any difficulty. Trypanosomes numerous in cerebro-spinal fluid.

May 1. Much worse. Can hardly walk at all. Tremor very distinct.

May 18. Patient admitted to the sleeping sickness hospital. Cannot stand without support. Appetite bad ; has lost flesh considerably of late. Much expectoration of very watery sputum. Pulse 120. Dulness of base of both lungs. Marked œdema of feet. Extreme tremor of tongue, lips, and hands. Knee jerks brisk. Pupils normal.

June 11. Patient is bedridden. Eats very little. Lies in a semi-conscious state the whole day. Extreme tremor when aroused. Complains of pain in his chest. He is getting very thin.

June 18. He is getting gradually weaker. Temperature remains between 95-96°. There is marked œdema around both eyes, of both feet and of the back.

June 26. Patient died at 4.30 a.m.

The following table shows the presence or absence of trypanosomes in the blood, lymphatic glands and cerebro-spinal fluid :—

Date.	Parasites in Blood.			Parasites in Glands.		Parasites in Cerebro-spinal Fluid.	
	Fil.	Mal.	Tryp.	Strept.	Tryp.	Strept.	Tryp.
1903.							
March 31	+	—
April 1	+
" 2	+
" 3	+
" 17	—
May 1	+	—
" 11	+	—
" 25	+	—
June 9	+	—
" 23	+	—
July 22	+	+
Aug. 18	+
Sept. 21	+	—
Nov. 9	+	—
Dec. 26	+	+

Date.	Parasites in Blood.			Parasites in Glands.		Parasites in Cerebro-spinal Fluid.	
	Fil.	Mal.	Tryp.	Strept.	Tryp.	Strept.	Tryp.
1904.							
Feb. 1	—
March 21	+	...	+	...	—
June 7	+	...	+	...	+
July 18	—	...	+	...	+
Aug. 25	+	...	+	...	+
Oct. 2	+	...	+	...	+
Dec. 13	+	—	+	—	+
1905.							
Jan. 3	+	—	+	—	+
Feb. 8	—	—	+
April 8	—	—	+	—	+
May 1	—	—	+
" 18	—	—	+
" 27	—	—	+
" 30	+	—	+	—	+
June 8	—	—	+
" 17	+	—	+
" 21	—	—	+
" 26	—	+	...	+	+

Since January, 1905, patient's temperature chart has shown constant slight evening elevations of temperature, which continued almost without interruption to the middle of May. During the third week of May there was a sharp rise, the temperature reaching 103°. The temperature became sub-normal at the beginning of June, and remained in this condition until death.

June 26. *Post-mortem* examination 1½ hours after death.

The body is that of a well-nourished man, but rather thin. There is general enlargement of the superficial lymphatic glands. There is marked œdema around both eyes, more especially the right, and also œdema of the feet. The pupils are equal and normal.

Brain.—The dura-mater is adherent in places to the calvarium. The pia-arachnoid shows areas of thickening and opacity. The whole appearance of the brain is typical of sleeping sickness. Active motile trypanosomes are present in the cerebro-spinal fluid in moderate numbers. Stained films of this cerebro-spinal fluid deposit show a vacuolated trypanosome and a few scattered diplo-cocci. Trypanosomes can also be seen in stained films made from scrapings of the brain surface.

Lungs.—Are both very œdematous. The left pleural cavity contained twelve ounces of fluid. Trypanosomes could not be found in this fluid.

Lymphatic glands.—Are enlarged in the cervical and axillary regions. Some of these enlarged glands are hæmorrhagic on section. Trypanosomes could not be found in stained films made from the gland-juice.

The other organs of the body were all carefully examined and showed no abnormality.

Remarks.—This man originally came under observation as a case of Trypanosoma fever more than two years ago, since which time he has been continually under observation. His temperature has been taken every day, and his blood, glands and cerebro-spinal fluid have been regularly examined. Trypanosomes have been constantly found in either his blood, glands or cerebro-spinal fluid from the very beginning. For the last year, trypanosomes have been found in his cerebro-spinal fluid at every examination. Up to June, 1904, his temperature chart showed irregular periods of

fever lasting for a day or two, an interval of one or two weeks of normal temperature usually intervening. From June, 1904, up to within a short time of death there has been constant daily fever, generally more marked towards evening and varying between 99° and 101°.

The patient's original slight symptoms very gradually increased in severity, the slight glandular enlargement became more marked, œdema of various parts of his body appeared, a constant daily pyrexia replaced the former irregular attacks of fever, and he became stupid, drowsy and unfit for any work. The original slight tremor grew very marked indeed; trypanosomes appeared in his cerebro-spinal fluid, and were afterwards constantly found there. Coma slowly developed, his temperature became sub-normal, and he died a typical case of sleeping sickness, amply confirmed at the autopsy.

CASE 63. KUMSARSABBA. MALE. AGE 25 YEARS.

Policeman. Nubian.

March 28, 1903. Admitted to hospital with fever. Temperature 102°. Says that he has never been ill before, now complains of headache.

History.—Has been in the police force for the last 11 months. Comes from Buddu. Does not know anybody with sleeping sickness. Is well-made and looks healthy. Tongue furred and said to be slightly tremulous. Lymphatic glands not enlarged in cervical region, but slightly in the groins. Walk normal. Speech also normal. No œdema of limbs or about the eyes. Heart and lungs normal. A blood-film examined by Dr. Baker showed the presence of trypanosomes.

March 30. Temperature has fallen to normal.

May 1. Temperature has remained normal for the last month. Patient seems quite well.

September 29. Patient says that he feels quite well. There are no signs of sleeping sickness. No headache or pain anywhere. Lymphatic glands are slightly enlarged in both posterior triangles, in axillæ and in both groins.

November 12. Condition unchanged. His cerebro-spinal fluid has now been examined six times, but trypanosomes have never been found in it. His temperature chart shows several sharp elevations of temperature to have occurred during the last eight months.

February 2, 1904. Patient remains in exactly the same state.

April 5. Lymphatic glands distinctly enlarged in left posterior triangle and in groin. Hands and tongue very slightly tremulous. Actively motile trypanosomes found in the gland-juice, examined to-day for the first time. Temperature remains about normal.

September 5. Glands enlarged as before; trypanosomes numerous in the gland-juice, but not present in the cerebro-spinal fluid, which is very clear and almost free from cellular deposit.

December 12. Temperature chart now shows slight daily elevations, which only rarely rise a degree or two above normal. General condition remains as before.

April 26, 1905. Glands enlarged as before. Slight œdema of both feet. Patient talks normally and says that he feels quite well. Actively motile trypanosomes present in the gland-juice. Tremor of hands and tongue very slight, if present at all. Temperature chart for the last four months still shows that patient's temperature is not quite normal, but that generally there is a slight evening rise.

July 20. Remains in exactly the same condition. Refuses to allow any more lumbar punctures to be performed, threatening to run away.

January 6, 1906. Temperaturo chart remains of the same character, showing a slight evening elevation. Trypanosomes are still present in the lymphatic glands and have always been found there at every examination. Patient looks well. He is reported to do his police work as well as ever. He complains of nothing.

March 1. Patient has been invalided from the police as not now fit for duty. Said by his native officer to have been formerly a very good shot. but to be now no good at all. Also reported to be lazy and careless. There is a heavy appearance about the man's eyes, though he says that he has no headache and feels well. His temperature chart has shown the same slight rise of an evening for the last three months. Tremor of the fingers is a little more marked than formerly. Patient has not lost flesh; he says his appetite is as good as ever. There is some fulness under the eyes, but no oedema anywhere else. Trypanosomes are still present in the gland-juice in considerable numbers, but cannot be found in a blood-film. He refuses to allow any examination of his cerebro-spinal fluid.

A photograph of Kumsarsabba has been taken to show his present healthy appearance in spite of the fact that trypanosomes have been continually found in either his blood or lymphatic glands for the last three years.

The following table shows the presence or absence of trypanosomes from the blood, glands and cerebro-spinal fluid of this patient :—

Date.				Parasites in Glands.		Parasites in Blood.			Parasites in Cerebro-spinal Fluid.	
				Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.
1903.										
March	28	+
May	7	—	...	—
"	16	—
"	19	—
June	25	+	...	+	...	—
July	28	+	...	+	...	—
Aug.	19	—
Sept.	29	+	...	—	...	—
Nov.	12	—	...	—	...	—
"	24	+	...	+
Dec.	27	+	..	—	...	—
1904.										
Feb.	2	+	...	+	...	—
April	5	+	—	...	—
Sept.	5	+	+	...	—
Dec.	12	+	—	...	—
1905.										
April	26	+	—	+	—
July	30	+	+	—	+
Dec.	20	+	+	—	—
1906.										
Jan.	6	+	—	—	—
March	1	+	+	—	—

In June, 1904, four Usoga prisoners were selected on account of typical gland-enlargement. Trypanosomes having been found in the glands of all of them, the men were placed in hospital and their temperatures were regularly taken. Their temperature charts showed irregular outbursts of fever every three or four

weeks, the temperature remaining normal during the intervening periods. Trypanosomes were generally to be found in their blood during these outbursts of fever. This state of things continued up to November, 1904.* At the present time one of these four men has died of sleeping sickness, one escaped and has not been heard of for the last year, while the two remaining are still alive and are under observation in our hospital. A detailed report of these cases follows :—

CASE 310. MONDU. MALE. AGE 25.

District, Usoga.

July 8, 1904. This case, selected from a group of prisoners, showed general enlargement of the lymphatic glands, but no other signs of sleeping sickness. The juice from a gland in the right posterior triangle of the neck was examined and found to contain many active trypanosomes.

July 10. Intramuscular injections of arsenious acid were commenced.

October 10. General health of the patient good. Temperature has every night been above normal, but only occasionally higher than 100°. Patient has put on weight considerably.

November 4. Trypanosomes cannot be found in the cerebro-spinal fluid. Temperature remains consistently above normal at night.

January 20, 1905. Arsenic treatment recommenced. Patient remains in exactly the same state. There is no tremor, no headache, and he complains of nothing. The temperature still keeps consistently above normal ; on two or three occasions it has run up to nearly 103°.

April 25. Arsenic treatment stopped. Temperature has not been influenced by the arsenic treatment ; it is still consistently above normal. Trypanosomes have not been found in the blood or glands for four months. Patient is, however, so fat that it is impossible to puncture the glands with certainty.

May 11. Trypanosomes found in the cerebro-spinal fluid to-day for the first time. No parasites to be found in a blood-film. Patient complains of headache, remains exceedingly fat, has a good appetite and sleeps and walks normally. He works every day at clearing the grounds with the other prisoners.

August 17. Patient seems to be getting lethargic ; he sits and lies about most of the day. There is slight tremor of the tongue and lips. He has not lost flesh, but remains exceedingly fat. Trypanosomes have been found in the cerebro-spinal fluid at every examination since May, but they have not been found in the blood since January. It is impossible to examine the glands. Temperature remains above normal as before, and there have been several sharp rises.

October 28. Patient is very distinctly more dull and lethargic. He can still walk but only in an uncertain manner. He does no work. He remains just as fat as formerly. He still eats well, but sleeps a great deal. Trypanosomes are regularly present in his cerebro-spinal fluid, and in increasing numbers.

November 23. Patient has become rather suddenly much worse. He is semi-conscious. His temperature has become sub-normal. He only eats and drinks when food is forced upon him. He is covered all over with itch.

December 6. State of coma is slowly deepening. There is no rigidity or paralysis or optic deviation. Pupils are equal. Cerebro-spinal fluid contains

* For detailed description of cases see Sleeping Sickness Report, No. VI., pages 50-64.

trypanosomes in large numbers. There is a great increase in the amount of cellular deposit on centrifuging the cerebro-spinal fluid. Trypanosomes are also very numerous in a blood-film (since January, 1905, parasites had not been found in this patient's blood).

December 22. Patient died at 5 p.m. this afternoon.

The following table shows the results of the examinations for parasites in the blood, glands, and cerebro-spinal fluid of this case from December 1, 1904 :—

Date.	Parasites in Glands.		Parasites in Blood.			Parasites in Cerebro-spinal Fluid.		As ₂ O ₃ in milligrammes.
	Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.	
Dec. 1...	—	—	—	—	—	None.
" 7...	—	—	—	—	—	"
" 31...	—	—	+	—	—	"
1905.								
Jan. 20...	—	—	—	—	+	10
" 24...	15
" 26...	—	—	—	—	—	20
" 30...	25
Feb. 2...	30
" 6...	—	—	+	—	—	30
" 8...	40
" 13...	—	—	—	—	—	40
" 17...	40
" 24...	35
March 3...	—	—	+	—	—	40
" 7...	45
" 13...	—	—	—	—	—	40
" 15...	40
" 17...	—	—	—	—	—	25
" 20...	15
" 25...	—	—	—	—	—	None.
April 29...	—	—	—	—	—	"
May 11...	—	—	—	—	—	—	+	"
" 18...	+	—	—	"
" 23...	—	—	—	"
June 3...	—	—	—	"
" 14...	—	—	—	...	+	"
" 21...	—	—	—	"
July 11...	—	—	—	...	+	"
" 22...	+	—	—	"
Aug. 17...	—	—	—	...	+	"
Sept. 23...	—	—	—	...	+	"
Oct. 28...	—	—	—	...	+	"
Dec. 6...	—	—	+	...	+	"
" 22...	—	—	—	+	+	"

From November, 1904, to the end of November, 1905, patient's temperature has been constantly about one-and-a-half or two degrees above normal. On three or four occasions bursts of fever lasting about forty-eight hours have occurred. On November 24, 1905, his temperature became sub-normal and remained so until death.

December 22. *Post-mortem* examination, half an hour after death.

The body is exceedingly fat. The superficial glands are impalpable, but on cutting down are found to be enlarged. The skin is dry and shows many scratch marks. The pupils are equal. The brain is congested and has the typical appearance of sleeping sickness. Trypanosomes can be found in the cerebro-spinal fluid in scanty numbers. Stained films of the various parts of the brain show that trypanosomes are present in the brain-nuclei, but cannot

be found in other parts. Sections of the brain cortex and nuclei both show well marked small-celled infiltration around the cerebral blood vessels. The other organs showed nothing worthy of note.

When first seen this man appeared to be in perfect health. As his cervical glands were larger than normal, these were examined with the result that trypanosomes were found in the gland-juice. When his temperature was taken twice a day, it was found that his evening temperature was nearly always about 100° . Trypanosomes were found in his blood on four occasions when he first came under observation. Afterwards, trypanosomes were not found in the blood until a fortnight before death, when they were numerous. Not until seven months before death were trypanosomes found in his cerebro-spinal fluid. When the parasites had once been found there, they were always found on subsequent examinations, and in increasing numbers, up to a fortnight before death. After death trypanosomes could be found in the brain and cerebro-spinal fluid, but only in quite scanty numbers.

The whole course of the latter part of the disease was quite typical of sleeping sickness. Sections of the brain showed a very marked infiltration of small cells around the blood vessels in its substance.

The man died 18 months after he first came under our observation.

For the first 14 months, but for the fact of the constant evening rise of temperature and of occasional sharp short attacks of fever, the man was well. The treatment with arsenic did not seem to influence the course of the disease.

CASE 302. TENWA. MALE. AGE 25.

District, Usoga.

June 7, 1904. Patient was selected from a group of prisoners from Usoga, on account of enlarged glands in the neck. He asserts that he is quite well. Beyond general glandular enlargement, there are no signs of sleeping sickness. The lymph from a gland in the left posterior triangle of the neck was examined and found to contain many active trypanosomes.

October 16. General condition has improved considerably since admission. Slight elevations of temperature have occurred from time to time. At these times parasites have appeared in the blood. Weight 10 st. 5 lbs.

December 9. Evening temperature nearly always now about 100° . Patient feels and looks well, and shows no symptoms of sleeping sickness.

April 15, 1905. Temperature shows the same persistent rise in the evening. This morning the temperature is 101.6° , and trypanosomes are present in the blood. General condition remains unchanged. Weight, 10 st. 10 lbs.

May 10. For the first time trypanosomes found in the cerebro-spinal fluid, which is quite clear and watery; there is only a very slight cellular deposit after centrifuging 20 cubic centimetres. Trypanosomes are not present in the blood.

September 23. Patient looks and feels as well as usual. There is no tremor and no loss of flesh nor symptoms of lethargy. There has been a continuous evening rise of temperature for a year.

January 11, 1906. Patient has not seemed quite so well lately. He is rather dull and stupid. His temperature chart still shows constant slight fever, but the variations are greater than formerly. There is no tremor. To-day his temperature has run up to 105° and trypanosomes are numerous in his blood.

Trypanosomes have been found in his cerebro-spinal fluid on four occasions since May, 1905, and on three examinations have proved negative.

The following table shows the presence or absence of parasites from his blood, glands, and cerebro-spinal fluid :—

Date.	Parasites in Glands.		Parasites in Blood.			Parasites in Cerebro-spinal Fluid.	
	Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.
Dec. 31	...	—	—	—	—
Feb. 13	...	—	+	—	—
" 18	—	—	—
March 14	...	—	—	—	—
" 17	...	—
April 15	+	—	+
" 20	...	—	+	—	—
May 4	...	—
" 10	+	—	—	...	+
" 16	—	—	—
" 27	+	—	—
June 3	+	—	—
" 21	+	—	—
July 10	+	—	—	...	—
" 23	+	—	—
Aug. 18	...	—	+	—	—	...	+
" 28	...	—	—	—	—
Sept. 23	...	—	—	—	—	...	+
Oct. 28	...	—	+	—	—	...	—
Dec. 6	...	—	—	—	—	...	—
Jan. 5	...	—	+	—	—	...	+
" 11	+	—	+

For the last 18 months patient's temperature has been constantly slightly above normal, varying between 99° and 101°. During this time there have been very occasional outbursts of high fever, lasting not more than 24 hours.

CASE 304. MANAWA. MALE. AGE 25.

District, Usoga.

June 12, 1904. This man was selected on account of enlarged glands in his neck. His general condition was good. Gland-juice examined and found to contain many active trypanosomes.

October 16. The general health of the patient was good.

January 1, 1905. Evening temperature varies between 99° and 100°. Trypanosomes have not been found in the blood or glands since September last. There are no symptoms of sleeping sickness.

January 24. Intramuscular injections of arsenious acid commenced.

February 28. Arsenic treatment stopped.

May 10. Cerebro-spinal fluid examined but trypanosomes not present.

June 16. Trypanosomes found in the cerebro-spinal fluid to-day for the first time. Temperature chart has shown a slight continual evening rise of temperature for the last eight months. Patient's general state remains as usual. There are no symptoms of sleeping sickness.

September 23. Condition good ; no symptoms of the disease. Trypanosomes cannot be found in either the cervical or axillary gland-juice. Glands are certainly not so much enlarged as they originally were.

January 10, 1906. Patient's condition remains unchanged ; his temperature chart presents the same characteristics as formerly. There are no symptoms of sleeping sickness. His cerebro-spinal fluid has been examined nine times, four times only with a positive result.

The following table shows the presence or absence of trypanosomes in his blood, glands and cerebro-spinal fluid and the amount of arsenic taken :—

Date.	Parasites in Glands.		Parasites in Blood.			Parasites in Cerebro-spinal Fluid.		As ₂ O ₃ in milligrammes.
	Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.	
1904.								
Dec. 1	+	—	—	
" 7	—	
" 31	+	—	—	
1905.								
Jan. 24	—	+	—	—	During Jan., 65. " Feb., 310.
Feb. 2	—	+	—	—	
May 10	—	+	—	—	...	—	
" 18	+	—	—	
June 3	—	+	—	—	
" 16	+	—	—	...	+	
" 21	—	—	—	
July 25	—	+	—	—	...	+	
Aug. 18	—	—	—	—	...	+	
Sept. 23	—	—	—	—	...	—	
Oct. 28	—	+	—	—	...	—	
Dec. 7	+	—	—	...	—	
1906.								
Jan. 5	—	+	—	—	...	+	

Patient's temperature has exactly resembled that of the previous case (Tenwa), showing a similar constant elevation of temperature with occasional outbursts of high fever.

V.—On the Treatment of Trypanosomiasis with Drugs in Men and in Animals.

i. IN MEN.

(1) Arsenic.

We give a full account of a few early cases of trypanosome infection which we have been able to keep more or less continually under arsenic. We have used throughout a solution of arsenite of soda and common salt of such a strength that one cubic centimetre of the solution contained four milligrammes of arsenious acid. At first the drug was given as an intramuscular injection into the buttock. A single large dose given in this way was repeated, as a rule, every 48 hours. As we found it very difficult to get natives to submit to these repeated injections, we have lately tried giving this same solution by the mouth in smaller but more frequent doses.

The following table shows that the trypanosomes generally disappear from the blood and glands when this arsenic treatment is first started, but that in the majority of cases the parasites reappear again. In two cases (No. 6 and 7) the parasites have not reappeared in the blood or glands up to the present, and the patients continue in good health. Case 9 is disappointing, trypanosomes are constantly to be found in the glands in spite of the increasingly large doses of arsenic which are given.

TABLE VI.

Table showing the effects of arsenic on Trypanosoma gambiense.

Name of Case.	Month in which observations were made.	Trypanosomes in the lymph glands.		Trypanosomes in blood.		Amount of arsenic as arsenious acid in milligrammes.
		No. of observations.	Results.	No. of observations.	Results.	
Mondu, 1 ...	1904.					
	Jan.	2	2—	2	1+ 1—	100
	Feb.	2	2—	2	2—	215
	March	4	4—	4	4—	205
Marco, 2 ...	Nov.	3	3+	3	3—	90
	Dec.	4	2+ 2—	4	4—	101
	1905.					
	Jan.	2	2+	1	1—	38
	Feb.	2	2+	2	1+ 1—	85
	March	3	2+ 1—	3	3—	150
	April	1	1+	1	1—	20
	May	4	4+	3	3—	101
	June	3	3+			133
	July	2	2+			65
	Aug.	1	1+			105
	Sept.	2	1+ 1—	2	2—	78
	Oct.	1	1+			25
	Nov.	1	1+			50
	Dec.	1	1+			10
Zigudegen-eamba, 3	Jan.	1	1+	1	1+	75
	Feb.	2	2—	2	2—	110
	March	4	3+ 1—	2	2—	140
	April	2	2+	2	2—	46
	May	5	3+ 2—	1	1—	126
Gabouleri, 4 ...	April	2	2+	2	1— 1+	122
	May	1	1—	1	1—	186
	June	4	2+ 2—	4	4—	216
	July	4	2+ 2—	3	3—	220
	Aug.	2	2—	2	2—	210
	Sept.	2	2—	2	2—	120
	Oct.	2	2+	2	2—	86
	Nov.	1	1+	1	1—	none
	Dec.	2	2+	1	1+	80

Name of Case.	Month in which observations were made.	Trypanosomes in the lymph glands.		Trypanosomes in blood.		Amount of arsenic as arsenious acid in milligrammes.
		No. of observations.	Results.	No. of observations.	Results.	
Francisco, 5 ...	1904.					
	June	2	2+			24
	July	1	1+	1	1—	150
	Aug.	2	2+	2	2—	192
	Sept.	1	1+	1	1—	160
	Oct.	1	1+	1	1—	224
Martini, 6 ...	June	2	2+	1	1—	36
	July	1	1+	1	1—	220
	Aug.	1	1—	1	1—	230
	Sept.	2	2—	1	1—	240
	Oct.	1	1—	1	1—	232
Jakoasi, 7 ...	Feb.	2	2+	2	2—	80
	March	4	4—	4	4—	415
	April	6 {	3— 3+	} 4	4—	348
	May	} 14	14—	14	14—	none
	June					
	July					
	Aug.					
	Sept.					
	Oct.					
	Nov.					
	Dec.					
Narain Singh, 8	June	1	1+	1	1—	34
	July	1	1+	1	1—	210
	Aug.	1	1—	1	1—	300
	Sept.	1	1+	1	1—	200
	Oct.	1	1+	1	1—	320
	Nov.	1	1+	1	1—	80
Ladha Singh, 9	April	3 {	1+ 2—	} 2	2—	126
	May	3	3+	3	3—	186
	June	1	1+	1	1—	240
	July	2	2+	2	2+	280
	Aug.	1	1+	1	1+	310
	Sept.	1	1+	1	1—	360
	Oct.	1	1+	1	1—	372
	Nov.	1	1+	1	1—	420
	Dec.	1	1+	1	1—	496

Cases 6, 7, 8, and 9 are now given in detail.

Cases 6 and 7 are interesting because arsenic seems to have had some considerable effect on their trypanosomes. Trypanosomes have not been found in case No. 7 for as long as ten months.

Cases 8 and 9 are of interest from the fact that the patients are both sepoys of the Indian contingent, and have only been in Uganda two years.

MARTINI. (No. 6.) MUGANDA BOY. 14 YEARS.

June 16, 1905. Lives in Entebbe, in shamba close to the lake-shore, near the Catholic mission. Sent up by the French fathers as a suspected case of sleeping sickness. Says that he sometimes has headache, but feels quite well now. Does not look ill. Says that he sleeps and eats well. There is no tremor. Patient does not seem dull or listless. There is marked enlargement of the cervical and axillary glands. Puncture left cervical gland. Trypanosomes are numerous in the gland-juice. Arsenic treatment started.

August 19. General condition remains good. Trypanosomes cannot be found in the glands to-day.

September 15. Condition as before; trypanosomes are still absent from the glands.

November 12. Patient having to leave for Kampala, arsenic treatment stops. His general condition good. Trypanosomes still absent from the glands. Pulse has always been about normal. No signs of sleeping sickness.

The following table shows the results of the blood and gland examinations, and also the amount of arsenic taken every month:—

Date.	Parasites in Glands.		Parasites in Blood.			Parasites in Cerebro-spinal Fluid.		Arsenious Acid in Milligrammes.
	Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.	
June 16	+	—	—	—	During June, 36.
" 21	+	
July 19	+	+	—	—	" July, 220.
Aug. 18	—	+	—	—	" Aug., 230.
Sept. 4	—	" Sept., 240.
" 15	—	—	—	—	" Oct., 232.
Oct. 12	—	
Nov. 12	—	+	—	—	

JAKOASI. MUGANDA MALE. (CHIEF MUGULA.) (No. 7.)

History.—Patient has lived in Entebbe all his life. Has been a porter for the last nine months. Says that he goes down to the lake-shore every day to wash his clothes about 2 p.m. Complains of fever, pains in the back of his head, and pain in the stomach for the last eight days.

February 21, 1905. *Condition.*—Tongue clean, not tremulous; no tremor of the lips or fingers. Patient has a heavy look about the eyes; walks normally. Says his appetite is good, that he has not vomited, that he does not feel sleepy, and that he only sleeps at night-time. Gland enlargement is marked in the cervical region, chiefly along posterior border of the sterno-mastoid, and at nape of neck. Glands are also enlarged in the right axilla, and slightly in both femoral regions. Glands are soft and movable. Joints are normal; there is no oedema of hands, feet, &c. Skin is normal, it does not itch. Pulse 88. Temperature 99.2°. Respiration normal. Gland-juice shows many actively motile trypanosomes. Blood-film is negative. Patient was started on injections of arsenic, which were given intramuscularly about every third day.

March 6. Trypanosomes cannot be found in the glands to-day. Patient's general condition remains unchanged.

April 6. Trypanosomes, which up to to-day could not be found in the glands, have now reappeared. General condition remains satisfactory. Patient says that he feels better, and has no pain anywhere.

April 18. Trypanosomes have disappeared again from the glands. Patient complains of nothing ; says that he can do his work as well as ever.

June 22. Patient well. Trypanosomes absent from glands.

August 8. Patient returned from Kampala, where he has been since the middle of June. He is not taking any arsenious acid now. Trypanosomes cannot be found in his glands or blood. Patient is in good health. Lymphatic glands of the neck do not seem as large as formerly.

October 27. Appears in good health. Temperature 98.4°. Pulse 80. Trypanosomes not found in gland-juice or in blood.

December 5. Patient continues in the same satisfactory state, and says that he feels well. Trypanosomes still absent from the glands and blood.

The following table shows the presence or absence of trypanosomes in the blood and glands, and also the amount of arsenious acid taken per month :—

Date.	Parasites in Glands.		Parasites in Blood.			Arsenious acid in milligrammes.
	Strept.	Tryp.	Fil.	Mal.	Tryp.	
Feb. 21	+	+	—	—	During Feb., 80.
" 23	+	+	—	—	
March 6	—	+	—	—	
" 11	—	—	—	—	During March, 415.
" 16	—	—	—	—	
" 29	—	+	—	—	
April 6	+	—	—	—	
" 8	+	—	—	—	During April, 348.
" 10	+	—	—	—	
" 18	—	—	—	—	
" 21	—	+	—	—	
" 29	—	—	—	—	
May 4	—	—	—	—	None.
" 11	—	—	—	—	"
" 27	—	—	—	—	"
June 2	—	+	—	—	"
" 10	—	—	—	—	"
" 22	—	—	—	—	"
Aug. 8	—	—	—	—	"
" 19	—	—	—	—	"
Sept. 1	—	—	—	—	"
" 12	—	+	—	—	"
Oct. 4	—	—	—	—	"
" 27	—	+	—	—	"
Nov. 15	—	—	—	—	"
Dec. 5	—	—	—	—	"

NARAIN SINGH. SEPOY INDIAN CONTINGENT, 4TH K.A.R. (No. 8).

History.—Is a sepoy of seven years service. Comes from Sialkot in the Punjab. Always had good health while in India. Arrived at Mombasa in good health in March, 1904. On arrival in Uganda, was 10 days at Mununyo on baggage guard, living in a large grass hut on the lake-shore in company with 20 other sepoys. (Mununyo, the port of Kampala, is infested with

Glossina palpalis.) He then came to Entebbe, where he lived in the Indian lines till January, 1905. While in Entebbe he was admitted to hospital as follows :—

April 13–16, 1904. Fever ; cause not diagnosed.

May 6–8, 1904. Fever (Malaria ?) ; blood not examined.

December 30–31, 1904. Abscess.

January 19–21, 1905. Fever ; cause not known.

January 26–28, 1905. Fever ; cause not known.

In February, 1905, he went to Kampala, where he again had fever.

June 22, 1905. Sent to us at Entebbe for examination with six other sepoys. Patient is thin, says that he is now quite well, but that he has had fever several times during the last four months. Is now doing ordinary duty, which he says that he can do easily. He has no pain ; eats and sleeps normally. Temperature 99°. Pulse 100. Respiration normal.

Tongue clean ; no tremor ; skin normal. Marked gland-enlargement on both sides of the neck and in both axillæ. Glands also enlarged in both groins, but only slightly. The glands are quite movable, soft and painless. There are no sores or scratches about the head or arms, and no œdema about the eyes or limbs. Blood examined with a negative result. Gland on right side of neck punctured ; trypanosomes found to be numerous in the gland-juice.

June 22. Patient put on injections of arsenious acid, given every other day, starting with 8 milligrammes, this dose being gradually increased.

July 3. Patient seems perfectly well. Complains of nothing. Temperature remains normal. Trypanosomes present in the glands.

August 8. Patient is now taking 20 milligrammes of arsenious acid every other day.

October 18. Temperature has been taken every four hours for the last fortnight. It is now seen to be not quite consistently normal, but shows a rise towards the middle of the day to about 99·4° or 99·8°. Patient remains in exactly the same state, insists that he is perfectly well. Trypanosomes are still present in his cervical glands.

November 13. Trypanosomes are still present in patient's glands ; a rat inoculated from patient's gland-juice, shows trypanosomes in its blood nine days later.

January 6, 1906. Patient's temperature has suddenly run up to 103·6°. His blood full of malaria (malignant tertian). Is given 10 grains quinine hypodermically. Trypanosomes not present in the blood.

The following table shows the result of the blood and gland examinations and also the amount of arsenious acid taken by the patient :—

Date.	Parasites in Glands.		Parasites in Blood.			Parasites in Cerebro-spinal Fluid.		Arsenic in Milligrammes.
	Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.	
June 22	...	+	—	—	—	During June, 34.
July 24	...	+	—	—	—	
Aug. 25	...	—	—	—	—	" Aug. 300.
Sept 22	...	+	—	—	—	" Sept. 300.
Oct. 18	...	+	—	—	—	" Oct. 320.
Nov. 13	...	+	—	—	—	" Nov. 80.
Dec. 20	...	+	—	—	—	None.

LADHA SINGH. SEPOY OF THE INDIAN CONTINGENT.

4th K. A. R. (No. 9.)

History.—General health in India good. Arrived at Mombasa in good health in March, 1904. Went straight to Kampala on arriving in Uganda. Was not on baggage guard at Mununyo with Narain Singh. From April, 1904, to January, 1905, lived in the Indian lines at Entebbe. While in Entebbe, was admitted to military hospital as follows:—

December 15–21, 1904. Fever; cause not known

January 18–22, 1905. Fever; cause not known. Says that he slept in the next bed to Narain Singh on this occasion.

January 28–31, 1905. Fever and headache; cause not known.

February, 1905. Sent to Kampala.

February 19. Came under the care of Capt. R. H. Price, I.M.S., with fever, headache and vomiting.

February 28. A slide of patient's blood, sent in to us, was found to contain numerous trypanosomes.

March 3. Patient transferred to the military hospital, Entebbe, and put under our care.

March 4. Patient is a tall, thin, well made man. To-day he says that he feels well. Pulse, 86; Temperature, $98^{\circ}4$; Respiration, normal. Says that his appetite is bad and that he has lost weight considerably. Suffers much from headache. Tongue rather furred, no tremor. No tremor of fingers. Knee jerks normal. Pupils normal. Edge of spleen can be felt just below costal margin. Liver impalpable. Pulse regular. Heart-sounds normal. Superficial glands on both sides of the neck and in both axillæ very considerably enlarged, soft, separate and movable. Gland on left side of neck was punctured, and trypanosomes were found to be numerous in the gland-juice. Blood-film shows trypanosomes in scanty numbers.

March 29. Temperature has run up again to 102° , having been about normal for the last ten days. Trypanosomes numerous in patient's blood.

April 18. Temperature up again to $102^{\circ}4$. Trypanosomes numerous in blood and in glands. In spite of the temperature patient says that he does not feel at all ill. An injection of eight milligrammes of arsenious acid was given at 11.15, and at 12.15 trypanosomes could not be found in a blood-film.

May 10. Patient's temperature has been quite normal for a month. He is taking arsenious acid regularly.

July 20. An acute iritis of the left eye has developed to-day. Given atropine. Pupil dilates to an oval shape. Arsenic omitted for a time.

July 28. Eye seems well again.

September 8. An acute iritis of the right eye has developed to-day. Dr. Moffat saw patient to-day and considered that the iritis was due to spirillum fever, probably contracted at the beginning of the year. Trypanosomes numerous in the glands.

September 23. Patient complains of pain in the right foot. Dorsum of foot is swollen; there is a red blush on the skin which disappears on pressure; distinct œdema over the painful area. Left foot quite normal. No other similar places on his body.

September 27. Patient has been kept lying down for the last four days and his foot has been treated with lead and spirit lotion. The foot is now apparently well again. Ever since the latter part of May, temperature has been slightly above the normal in the evening, generally being about 99.4 – 100° .

October 17. Patient says he feels very well. Has no headache. Eats and sleeps well. Is taking 12 milligrammes of arsenious acid a day. His evening temperature has not been above 99° for a month.

December 3. Herpes zona present, starting at the base of the coccyx and spreading over right buttock and in right groin. Patient says he feels quite well otherwise. His evening temperature has been twice over 100° during the last six weeks. He is now taking 16 milligrammes of arsenious acid a day. Trypanosomes still present in the glands.

January 1, 1906. Arsenious acid increased to 24 milligrammes a day. Patient is in good health, complains of nothing.

The following table shows the results of the blood examinations and also the amount of arsenious acid taken every month :—

Date.	Parasites in Glands.		Parasites in Blood.			Parasites in Cerebro-spinal Fluid.		Arsenious acid in milligrammes.
	Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.	
1905.								
Feb. 28	—	—	+	
March 4	+	—	—	+	
" 9	+	—	—	—	
" 13	—	—	—	
" 19	—	—	+	
April 7	—	—	+	During April, 126.
" 18	+	
" 25	—	—	—	—	
" 28	—	—	—	—	
May 6	+	—	—	—	" May, 186.
" 10	+	—	—	—	
" 31	+	—	—	—	
June 16	+	—	—	—	" June, 240.
July 7	+	—	—	+	
" 17	+	—	—	+	" July, 280.
Aug. 9	+	—	—	+	
Sept. 3	+	—	—	—	" Aug., 310.
Oct. 17	+	—	—	—	
Nov. 5	+	—	—	—	" Sept., 360.
Dec. 3	+	—	—	—	
								" Oct., 372.
								" Nov., 420.
								" Dec., 496.
1906.								
Jan. 3	+	—	—	—	
" 19	+	—	

This man's temperature chart showed irregular sudden outbursts of fever during February and March, 1905, when he first came under our notice. All April, May, and June, his temperature was practically normal. Since June, 1905, his temperature has never been above 100·5°, but very constantly shows a slight evening rise above the normal.

(2) *Tragaroth*. (Ehrlich.)

In January, 1905, a supply of *Tragaroth* reached us, kindly sent by Professor Dr. P. Ehrlich. So far we have only had an opportunity of using this drug on cases in which marked symptoms of sleeping sickness have appeared. We give the notes of a few of the cases in which the drug has been administered. In one case the drug was given as a subcutaneous injection. An objection to this treatment is that the

drug is only soluble in water to the extent of 1 per cent., and that the injection is therefore very bulky. In other cases the drug has been given by the mouth. We have never known Tragaroth to cause any ill effect even when taken in very large doses. We cannot say that the course of the disease has been influenced in any way in sleeping sickness patients who have taken this drug.

A native patient in an early stage of trypanosome infection, when possibly energetic treatment with drugs would be of some use, does not consider himself in any way ill and is very averse to a remedy of any description. If this remedy takes the form of painful injections often repeated, unless the patient really considers himself to be suffering from sleeping sickness, he will not submit to it. Up to the present time we have only been able to secure a very few prisoners in an early stage of trypanosome infection. These men are having their cerebro-spinal fluid examined regularly for the presence or absence of trypanosomes, and are not being treated with drugs.

BADINGO, KAVIRONDO. MALE. 38 YEARS.

Admitted October 3, 1904.

Has lived in Entebbe for the last five years, works close to the lake-shore. Has been ill for the last two months, and now complains of inability to do his work and of pains all over his body.

Facial expression dull; gait uncertain; skin very dry, but does not irritate. There is no œdema. Tongue clean, but very tremulous; there is tremor of the fingers and the knee jerks are brisk. No ankle clonus. Appetite good. Abdomen normal. Spleen cannot be felt. Heart and lungs appear normal. Superficial lymphatic glands generally enlarged and present the usual characters. Patient is thin, but not emaciated.

October 3, 1904. Cerebro-spinal fluid shows trypanosomes in moderate numbers. Trypanosomes are present in the gland-juice, but not in a blood film.

October 27. Two grammes of Trypanroth (Ehrlich) are injected under the skin into both axillæ in the form of a 1 per cent. solution in water. General condition as before. Patient shows only a very faint pink colour.

October 29. Pink colour much more marked. Trypanosomes cannot be found in the gland-juice.

November 25. Patient now much worse and cannot stand without support. The pink colouration from the Trypanroth has not yet disappeared. Cerebro-spinal fluid shows trypanosomes in about the same numbers as before. Fluid is more cellular than normal.

December 28. Patient has not got much worse during the last month. His temperature rose from sub-normal to 100·2°. Trypanosomes present in a blood-film, and in the cerebro-spinal fluid.

January 21, 1905. Patient lies in a stupor, cannot speak, can only just swallow. Cerebro-spinal fluid sterile, and contains trypanosomes in scanty numbers.

January 29. Patient died at 2 p.m.

The following table shows the presence or absence of trypanosomes in the blood, glands, or cerebro-spinal fluid :—

Date.	Parasites in Blood.			Parasites in Glands.		Parasites in Cerebro-spinal Fluid.		Trypanoth in Grammes.
	Fil.	Mal.	Tryp.	Strept.	Tryp.	Strept.	Tryp.	
1904.								
Oct. 3 ...	—	—	—	—	+	—	+	...
" 27	—	+	2
" 28	—	+
" 29 ...	—	—	—	—	—
Nov. 5	—	+
" 18 ...	—	—	+	—	+
" 25 ...	—	—	—	—	+	—	+	...
Dec. 14	+
" 28 ...	—	—	+	—	+	—	+	...

A *post-mortem* examination showed the brain to be very firm and fresh-looking ; the ground-glass appearance of cortex well marked and chiefly vertical in its distribution. Cerebro-spinal fluid is increased in amount, and there is slight flattening of the convolutions. Active trypanosomes are present in the cerebro-spinal fluid. Heart, normal ; lungs, no pleurisy, three triangular-shaped hæmorrhages (infarcts?) at apex of right lung ; stomach, two well-marked patches of superficial ulceration on lesser curvature, ulcers small and lie on the folds of the stomach ; kidneys, liver, and spleen are all normal. Superficial glands are markedly enlarged in every region ; glands are not suppurating ; mesenteric glands appear normal.

The injection of the Trypanoth had only a slight temporary effect on the parasites in the peripheral circulation.

TUMBO. MALE. AGE 12.

District, Entebbe, Uganda.

February 27, 1905. Admitted to hospital. Patient says that for the last year he has been in the service of a resident at Entebbe. One of the other servants says that patient has been drowsy and stupid for the last two months. Patient is a short fat boy with a heavy dull look about the eyes. His speech is slow but distinct. He can walk normally. He complains of headache and of occasional pain in his stomach. There is slight tremor of the tongue and fingers. There is well marked gland enlargement in the cervical and axillary regions. Trypanosomes are present in the blood and gland-juice. Pulse, 80 ; temperature, 99·4°. Treatment with Tragaroth commenced ; drug given by the mouth in water.

March 6. Patient seems more drowsy than on admission. Trypanosomes are present in the cerebro-spinal fluid. There is a very marked increase of white cells in this fluid which are nearly all mono-nuclear.

March 16. Patient has now taken 60 grammes of Tragaroth by the mouth. His sclerotics are distinctly pink.

March 26. Patient has now taken more than 80 grammes of Tragaroth ; trypanosomes are still present in the gland-juice.

March 30. Patient is much worse. He is very tremulous and can hardly walk.

April 10. Complains of pain in the right hip, right knee and wrist. Purulent conjunctivitis of both eyes.

April 19. Trypanosomes are present in the cerebro-spinal fluid in increased numbers. Patient is moribund.

April 23. Died at 9 a.m.

The following table shows the presence of trypanosomes in the blood glands and cerebro-spinal fluid, and also the amount of tragaroth given :—

Date.	Parasites in Blood.			Parasites in Glands.		Parasites in Cerebro-spinal Fluid.		Tragaroth in Grammes.
	Fil.	Mal.	Tryp.	Strept.	Tryp.	Strept.	Tryp.	
1905.								
Feb. 27 ...	—	—	+	—	+	3
March 2	6
" 6 ...	—	—	+	—	+	—	+	9
" 7	6
" 9	6
" 10	—	+	5
" 11	—	+	5
" 12 ...	—	—	+	5
" 13	5
" 14	—	+	5
" 15	5
" 16	—	+	2
" 17 ...	—	—	—	2
" 18	—	+	3
" 20 ...	—	—	—	—	+	3
" 21	3
" 22	3
" 24	3
" 26	3
" 28	3
April 1 ...	—	—	+	—	+	3
" 3 ...	—	—	+	3
" 6 ..	—	—	—	—	+
" 10 ...	—	—	—	—	+
" 12 ...	—	—	—
" 15 ...	—	—	—	—	+
" 19 ...	—	—	—	—	+	—	+	...
								91 grms.

A *post-mortem* examination made half-an-hour after death. The body is still fat; there is much muco-purulent conjunctivitis; the red colouration caused by the Tragaroth has disappeared. Lungs, normal; heart, normal; pericardium contains a little blood-stained fluid. Trypanosomes are not present in this fluid. Spleen weighs 9 ounces; some increase of fibrous tissue in its substance. Surface of the brain is quite typical of sleeping sickness. The cerebro-spinal fluid contains trypanosomes in considerable numbers. The surface of the brain and the cerebro-spinal fluid are sterile.

HAMESI. MALE. AGE 30.

District, Jinja, Usoga.

November 26, 1904. Admitted to hospital. Has lived at Jinja all his life. Has been a prisoner at Entebbe gaol for the last four months. Complains of headache and pains all over his body for the last two months. Patient looks somewhat dull and apathetic, his eyeballs are puffy and cedematous. There is no tremor. Liver and spleen are not palpable. The glands on both sides of neck and in the right axilla are enlarged. Trypanosomes are present in the gland-juice in large numbers, scantily present in a blood-film, and not present in the cerebro-spinal fluid.

December 28. Condition unaltered. Trypanosomes scantily present in the cerebro-spinal fluid. Patient complains of nothing.

February 24, 1905. Trypanosomes are present in the glands, blood and cerebro-spinal fluid. Treatment with Tragaroth commenced.

March 11. Patient has now had about 50 grammes of Tragaroth, by the the mouth. Sclerotics are pink.

April 6. Patient has now had 100 grammes of Tragaroth; the colouration from the drug is quite marked, but trypanosomes are still present in his glands.

April 18. Treatment with arsenic commenced.

April 27. He has had 70 milligrammes of arsenic in the last ten days. Trypanosomes have disappeared from the lymphatic glands.

May 13. Lumbar puncture again performed. The cerebro-spinal fluid is under considerable pressure. There is an increase of white cells in the deposit left after centrifuging the fluid. Trypanosomes are present. Trypanosomes cannot be found in either the blood or gland-juice. Patient has been taking arsenic regularly although not in such large doses as formerly.

May 30. Patient keeps to his bed much more than formerly and is now distinctly drowsy. Temperature has been subnormal on several occasions.

June 17. The drowsiness is steadily increasing. There is only slight tremor of the fingers. Trypanosomes are present in the cerebro-spinal fluid in increased numbers.

July 3. Patient is quite unconscious. Trypanosomes are still present in the cerebro-spinal fluid.

July 5. Patient died at 11 p.m.

The following table shows the presence or absence of trypanosomes in the blood, glands, or cerebro-spinal fluid, also the amount of arsenic and Tragaroth administered :—

[illegible]

Date.	Parasites in Blood.			Parasites in Glands.		Parasites in Cerebro-spinal Fluid.		Tragaroth in Grammes.
	Fil.	Mal.	Tryp.	Strept.	Tryp.	Strept.	Tryp.	
1905.								Arsenic in Milli-grammes.
April 12	—	—	—	—	+
" 18	—	+	16
" 20	—	+	22
" 25	—	+	32
" 27	—	—	16
" 29	—	—	12
May 1	—	—	16
" 5	—	—	10
" 7	15
" 9	20
" 11	20
" 13	—	—	—	—	+	—	+	...
" 15	—	—	—	—	+	12
" 17	15
" 18	—	—	—
" 19	15
" 24	—	15
June 1	—	—	—	..	+
" 8	—	—	—	...	+
" 15	—	—	—	...	+
" 17	—	—	+	—	+	—	+	...
" 21	—	—	—	—	+
July 3	—	—	—	—	+	—	+	...
" 5	—	—	—	+	—	+	+	...
								236 mgrms.

July 6. *Post-mortem* examination made nine-and-a-half hours after death. Body is very wasted and the eyes sunken. There is no œdema. The pupils are equal. There is general enlargement of the superficial lymphatic glands. Several opaque thickened patches are present on the pia-arachnoid, especially on the superior surface of the brain. Trypanosomes can be seen in smears of the brain-substance in scanty numbers. The stomach shows numerous small hæmorrhages on its internal surface. The spleen weighs 10 ounces. There is a marked increase of fibrous tissue on section of this organ. The cervical and axillary glands show general enlargement. Many of the glands are hæmorrhagic. Trypanosomes cannot be found in the gland juice. The other viscera appear healthy.

PAUL WAGANDA. MALE. 20 YEARS.

Lives in Kampala, but has been in Entebbe for the last eight months, where he lives near the French mission. Says that he has been ill for the last three weeks. Complains of pain in the limbs and back.

February 27, 1905. Patient says that he has been bitten by tsetse flies when he has gone down to the lake-shore to wash his clothes. He is well-nourished and looks well. Says that he has never had fever; that his appetite is good; that, except for the pain, he feels quite well; that he can do his work as well as ever, and that he only sleeps at night and does not feel drowsy during the day. Skin normal; no œdema. Pupils equal. Knee jerks normal. There is no tremor. Gland enlargement well-marked in cervical region on both sides, also in right axilla. Both epitrochlear glands enlarged. Temperature 99°. Pulse 88. Respiration normal. Gland juice shows many

actively motile trypanosomes, but these are absent from a blood-film. Patient is given 4 grammes of tragaroth, dissolved in water, and flavoured with peppermint.

March 7. Trypanosomes present in blood and gland. Colour of mucous membranes unaltered.

March 20. Patient has had 52 grammes of tragaroth. The sclerotics have now a distinct red colour. Trypanosomes are present in the glands.

April 1. Patient's glands are still full of trypanosomes. He refuses to take any more medicine. Sclerotics are still a pink colour.

June 16. Glands show numerous trypanosomes. Patient is very dull and stupid. Tongue is slightly tremulous. He refuses to come into hospital.

The following table shows the results of the blood and gland examinations, and the amount of tragaroth taken by this patient :—

Date.	Parasites in Blood.			Parasites in Glands.		Parasites in Cerebro-spinal Fluid.		Tragaroth in Grammes.
	Fil.	Mal.	Tryp.	Strept.	Tryp.	Strept.	Tryp.	
1905.								
Feb. 27 ...	—	—	—	—	+	4.5
March 2	4
„ 3	4
„ 4	5
„ 5	5
„ 7 ...	—	—	+	—	+	5
„ 9	5
„ 11	5
„ 14	5
„ 17	5
„ 20 ...	—	—	—	—	+	5
April 1 ...	—	—	—	—	+	4
June 16 ...	—	—	—	...	+
								56.5 grms.

ii. IN ANIMALS.

(1) *Arsenic.*

Experiments were first conducted to discover the minimum lethal dose of arsenious acid for the species of monkey which we commonly use in our experiments. Eight monkeys were obtained and weighed, and then given varying doses of a solution of arsenious acid of a strength of two milligrammes of arsenious

acid to the cubic centimetre. The drug was administered by subcutaneous injection. The following table gives the results of these experiments :—

TABLE VII.

No. of Animal.	Weight of Animal in kilogrammes.	Actual dose of Arsenious Acid given.	Ratio of Weight in grammes of animal per milligramme of Arsenious Acid.	Result.
A.	2.04	10 milligrammes	1 milligramme per 200 grammes	Died.
B.	1.24	5.5 "	1 " 225 "	Died.
C.	2.5	10 "	1 " 250 "	Died.
D.	1.24	5 "	1 " 250 "	Recovered.
E.	1.24	5 "	1 " 250 "	Recovered.
F.	1.23	5 "	1 " 300 "	Recovered.
G.	4.8	12 "	1 " 400 "	Recovered.
H.	3.52	7 "	1 " 500 "	Recovered.

From the above experiments it was found that a dose of arsenious acid in the proportion of one milligramme of arsenious acid per 250 grammes weight of monkey was the minimum lethal dose.

We give the details of four experiments in treating monkeys already infected with the trypanosome of sleeping sickness. Although arsenious acid was given in doses which were often repeated and in quantities not far short of the minimum lethal dose, yet in no case were we certainly able to cure the monkey. Experiment 415 was the most hopeful; trypanosomes had been absent from this animal's blood for nearly three months as the result of the arsenic, and the animal was in good health when we lost him, as recorded. Experiment 370 is interesting as it shows that trypanosomes may return to the peripheral circulation, after a two months' absence, as a result of the treatment.

EXPERIMENT 405. MONKEY (*Cercopithecus* sp.) WEIGHT 3.85 KILOS.

May 23, 1905. 2 cubic centimetres of cerebro-spinal fluid taken from a case of sleeping sickness are injected subcutaneously into this monkey. Trypanosomes are not found in the blood.

July 1. Trypanosomes have appeared in the blood to-day for the first time

July 11. Arsenic treatment commenced. 4 milligrammes of arsenious acid are given equal to 1 milligramme per 960 grammes monkey.

August 15. Animal has now had 17 milligrammes of arsenious acid during the last month. General condition remains satisfactory. Treatment stopped.

September 12. Trypanosomes have re-appeared in the blood to-day.

December 10. Animal died to-day.

Post-mortem. Body rather emaciated. All the viscera appear healthy. Spleen not enlarged. Lymphatic glands normal. Sections of brain do not show any small-celled infiltration. Trypanosomes were present in the blood up to the time of death in scanty numbers.

The following table shows the presence or absence of trypanosomes from the blood and also the amount of arsenious acid given :—

Date.	Parasites in Blood.		Arsenious Acid in milli-grammes.	Date.	Parasites in Blood.		Arsenious Acid in milli-grammes.
	Mal.	Tryp.			Mal.	Tryp.	
1905.							
May 23	—	...	Aug. 8	—	...
" 29	—	...	" 15	—	3
June 3	—	...	" 24	—	...
" 10	" 30	—	...
" 21	Sept. 11	+	...
" 26	" 12	+	3
July 1	+	...	" 20	—	...
" 7	+	...	" 26	—	...
" 11	+	4	Oct. 3	—	...
" 16	—	...	" 10	+	...
" 20	+	3	" 20	+	...
" 25	+	3	Nov. 12	+	...
" 30	—	...	" 24	+	...
Aug. 6	+	...	Dec. 10	+	...

EXPERIMENT 415. MONKEY (*Cercopithecus sp.*). WEIGHT 1·81 KILOS.

May 23, 1905. 2 cubic centimetres of cerebro-spinal fluid from a case of sleeping sickness injected subcutaneously. Trypanosomes absent from blood.

June 13. Trypanosomes have been constantly present in the blood up to to-day. Arsenious acid now administered in doses of 4 milligrammes, which equals 1 milligramme per 450 grammes monkey.

July 20. Animal has had 12 milligrammes of arsenious acid since the treatment was started. Arsenic stopped.

September 8. Animal eaten by a jackal in the night. Trypanosomes had not been found in the animal's blood since the arsenic treatment was started.

The following table shows the presence or absence of trypanosomes from the animal's blood, and also the amount of arsenious acid given :—

Date.	Parasites in Blood.		Arsenious Acid in milli-grammes.	Date.	Parasites in Blood.		Arsenious Acid in milli-grammes.
	Mal.	Tryp.			Mal.	Tryp.	
1905.				1905.			
May 23	—	...	July 16	—	...
June 7	+	...	" 20	—	2
" 13	+	4	" 25	—	..
" 14	—	...	" 30	—	...
" 24	—	...	Aug. 6	—	...
July 1	—	4	" 15	—	...
" 7	—	...	" 24	—	...
" 10	—	2	Sept. 8	—	...

EXPERIMENT 370. MONKEY (*Cercopithecus sp.*).

April 5, 1905. A few drops of blood from monkey 350, containing numerous trypanosomes, were injected into this animal.

April 10. Trypanosomes have appeared in the animal's blood to-day for the first time.

May 14. Trypanosomes have been constantly present in this animal's blood up to to-day. Weight of animal is 1.72 kilogrammes. Injected subcutaneously arsenious acid 4 milligrammes, which equals 1 milligramme per 400 grammes monkey.

May 15. Monkey seems sick to-day, and has been purged freely in the night. Trypanosomes cannot be found in the blood to-day.

July 10. Trypanosomes have reappeared in the animal's blood to-day. For the last two months parasites have not been found in the blood.

August 8. Animal found dead this morning. At the autopsy it was found that the animal's rectum had been perforated by the constant use of the clinical thermometer. There was much peritonitis present, otherwise all the viscera were healthy.

The following table shows the presence or absence of trypanosomes from the animal's blood, and also the amount of arsenious acid given :—

Date.	Parasites in Blood.		Arsenious Acid in milligrammes.	Date.	Parasites in Blood.		Arsenious Acid in milligrammes.
	Mal.	Tryp.			Mal.	Tryp.	
1905.				1905.			
March 13	—	...	May 31	—	3
" 22	—	...	June 7	—	3
April 5	—	...	" 12	—	...
" 10	+	...	" 18	—	...
" 15	+	...	" 26	—	...
" 21	+	...	" 30	—	...
" 28	+	...	July 10	+	3
May 5	+	...	" 16	—	...
" 14	+	4	" 20	—	...
" 15	—	...	" 30	—	...
" 24	—	3	" 4	—	...
" 29	—	..	" 8	—	...

This monkey was treated with frequently repeated large doses of arsenious acid. Trypanosomes disappeared from the blood for two months, but reappeared again as soon as the treatment was given up for a while.

EXPERIMENT 421. MONKEY. (*Cercopithecus sp.*). WEIGHT 1.04 KILOS.

May 31, 1905. 3 cubic centimetres of cerebro-spinal fluid taken from "Wasaneri," a case of advanced sleeping sickness, were injected into this animal in whose blood trypanosomes were ascertained to be absent.

June 13. Trypanosomes have appeared in the blood to-day for the first time.

July 11. Trypanosomes have now been present in the animal's blood for more than a month. 3 milligrammes of arsenious acid (=1 milligramme per 350 grammes monkey) were injected.

July 12. Trypanosomes have disappeared from the blood.

July 25. Monkey has had 7 milligrammes of arsenious acid in 14 days. Trypanosomes have remained absent from the blood.

September 12. Trypanosomes have reappeared in the animal's blood to-day, having been absent for two months.

September 26. Monkey has had six additional milligrammes of arsenious acid during the last fourteen days. Trypanosomes have again disappeared from the blood.

November 23. Trypanosomes have reappeared to-day, having been absent for 2½ months. Animal remains in good health.

The following table shows the results of the blood examinations, and the amount of arsenious acid given :—

Date.	Trypano- somes in Blood.	Arsenious Acid in Milli- grammes.	Date.	Trypano- somes in Blood.	Arsenious Acid in Milli- grammes.
1905.			1905.		
May 31 ...	—	...	Sept. 12 ...	+	3
June 13 ...	+	...	" 19 ...	—	...
" 24 ...	+	...	" 26 ...	—	3
July 11 ...	+	3	Oct. 3 ...	—	...
" 16 ...	—	...	" 20 ...	—	...
" 20 ...	—	2	" 29 ...	—	...
" 25 ...	—	2	Nov. 16 ...	—	...
" 30 ...	—	...	" 23 ...	+	...
Aug. 6 ...	—	...	Dec. 1 ...	—	...
" 13 ...	—	...	" 14 ...	—	...
" 24 ...	—	...	" 18 ...	+	...
" 31 ...	—	...			

Has arsenic any value as a prophylactic against the trypanosome of sleeping sickness in the case of monkeys?

We give the details of some experiments which were conducted to determine whether a monkey which was under the influence of arsenic could yet be infected with the trypanosome of sleeping sickness. Seven monkeys were used in these experiments. One of them was kept as a control, and was simply inoculated with a similar dose of cerebro-spinal fluid as was given to the other monkeys which were under the influence of arsenic. The control monkey showed trypanosomes in its blood 23 days after inoculation. Three of the other monkeys showed trypanosomes in their blood in spite of the previous doses of arsenious acid, but in these the appearance of the trypanosomes in the blood was much delayed. Two of the animals never showed trypanosomes in their blood, and in their cases, no doubt, the arsenic did protect the animals from infection; but in these two cases very large and dangerous doses of arsenious acid had been given, and the animals were made seriously ill by the drug. A similar dose given to the sixth and last monkey proved fatal. From these experiments we are brought to the conclusion that ordinary safe doses of arsenic given to monkeys before inoculation with human trypanosomes have little or no power in protecting the animals from subsequent infection.

EXPERIMENT 336. MONKEY (*Cercopithecus sp.*). WEIGHT 1.24 KILOS.

December 3, 1904. 5 milligrammes of arsenious acid were injected subcutaneously, which equals 1 milligramme per 250 grammes monkey.

December 4. Animal has had a good deal of diarrhœa in the night.

December 6. 4 milligrammes of arsenious acid administered.

December 19. 4 milligrammes of arsenious acid given.

December 21. 3 cubic centimetres of cerebro-spinal fluid were injected subcutaneously from a case of sleeping sickness (Abyabu), containing numerous trypanosomes.

February 13. Monkey is rather thin but otherwise healthy. Trypanosomes have not yet appeared in the blood.

February 21. Trypanosomes have appeared in the blood to-day for the first time (62 days after inoculation).

The following table shows the results of the blood examinations, and the amount of arsenious acid given :—

Date.	Parasites in Blood.		Parasites in Cerebro-spinal Fluid.		Arsenious Acid in milligrammes.
	Mal.	Tryp.	Strept.	Tryp.	
1904.					
Dec. 3	5
" 16	4
" 19	4
" 21	Inoculated with trypanosomes.				...
" 30	—	—
1905.					
Jan. 5	—	—
" 13	—	—
" 24	—	—
" 30	—	—
Feb. 8	—	—
" 13	—	—
" 21	—	+

The arsenic evidently prolonged the incubation period of the disease in this case.

EXPERIMENT 347. MONKEY (*Cercopithecus sp.*). WEIGHT 1,920 GRAMMES.

December 12, 1904. 4 milligrammes of arsenious acid, *i.e.*, 1 milligramme per 480 grammes monkey, were injected.

December 19. 6 milligrammes of arsenic, *i.e.*, 1 milligramme per 320 grammes monkey, were injected. Blood examined; trypanosomes are absent.

December 21. Injected subcutaneously 3 cubic centimetres of cerebro-spinal fluid from sleeping sickness case (Abyabu), containing numerous trypanosomes.

January 30. Trypanosomes appeared in the blood for the first time to-day, 40 days after inoculation.

March 20. Animal died to-day

The following table shows the presence or absence of trypanosomes in the blood :—

Date.					Parasites in Blood.		Parasites in Cerebro-spinal Fluid.		Arsenious Acid in milligrammes.
					Mal.	Tryp.	Strept.	Tryp.	
1904.									
Dec.	12	4
"	19	+	—	6
"	21	Inoculated with trypanosomes.				...
"	30	+	—
1905.									
Jan.	5	+	—
"	13	+	—
"	23	+	—
"	30	+	+
Feb.	5	+	+
"	8	+	+
"	13	+	+
"	17	+	+
"	21	+	+
March	1	+	+
"	8	+	+

Post-mortem examination (eight hours after death) Animal thin and very anæmic. No glandular enlargement. Trypanosomes not present in a blood-film. All the organs seem healthy, but anæmic. Spleen somewhat enlarged. Intestines contain a long tape-worm. Brain appears normal. No trypanosomes in the cerebro-spinal fluid.

EXPERIMENT 348. MONKEY (*Cercopithecus sp.*). WEIGHT 1,020 GRAMMES.

December 19, 1904. Injected 4 milligrammes arsenic, which equals 1 milligramme per 255 grammes monkey.

December 21. Animal ill. Extensive purging. Injected 3 cubic centimetres cerebro-spinal fluid from case of sleeping sickness (Abyabu) containing numerous trypanosomes.

December 23. Animal found dead this morning.

Post-mortem. Stomach shows marked patches of erosion; contains some altered blood. Liver, pale; has a flea-bitten appearance. Intestines show many inflamed patches. Trypanosomes are absent from the blood. This animal almost certainly died from the effects of the arsenic, given 3½ days previously.

EXPERIMENT 342. MONKEY (*Cercopithecus sp.*). WEIGHT 1,460 GRAMMES.

December 7, 1904. A maximum dose of arsenic—6 milligrammes (which equals 1 milligramme per 243 grammes monkey)—was injected.

December 8. Animal very weak and ill, has had much diarrhoea in the night.

December 12. Animal seems well again. Arsenic 4 milligrammes.

December 19. Arsenic 6 milligrammes.

December 21. Injected subcutaneously, three cubic centimetres of cerebro-spinal fluid from sleeping sickness case (Abyabu), containing numerous trypanosomes.

March 24. Animal's blood has been examined carefully every week since the day of inoculation. Trypanosomes have never been found in the blood. Animal, though thin, remains in good health.

The following table shows the dates and result of the blood examinations :—

Date.	Parasites in Blood.		Parasites in Cerebro-spinal Fluid.		Arsenious Acid in milligrammes.
	Mal.	Tryp.	Strept.	Tryp.	
1904.					
Dec. 7	6
" 12	4
" 19	+	—	6
" 21	Inoculated with trypanosomes.				...
" 30	+	—
1905.					
Jan. 5	+	—
" 13	+	—
" 23	+	—
" 30	+	—
Feb. 8	+	—
" 13	+	—
" 21	+	—
March 1	+	—
" 8	+	—

EXPERIMENT 349. MONKEY (*Cercopithecus sp.*). WEIGHT 1,030 GRAMMES.

December 19, 1904. Injected arsenic 4 milligrammes, *i.e.*, 1 milligramme per 260 gramme Monkey.

December 21. Animal ill. Some diarrhœa. Injected subcutaneously 3 cubic centimetres cerebro-spinal fluid from case of sleeping sickness (Abyabu), containing numerous trypanosomes.

December 30. Animal seems to have recovered from the arsenic. Trypanosomes are absent from the blood.

February 4. Animal died to-day. Blood has been examined every week, but trypanosomes have never been found in it. This animal stood captivity badly, and has got progressively thinner. There is a large sore on it's abdomen where the collar was attached.

The following table shows the result of the blood examinations :—

Date.				Parasites in Blood.		Parasites in Cerebro-spinal Fluid.		As ₂ O ₃ in milligrammes.
				Mal.	Tryp.	Strept.	Tryp.	
1904.								
Dec.	19	—	—	4
"	21	Inoculated with trypanosomes.				...
"	30	—	—
1905.								
Jan.	5	—	—
"	13	—	—
"	24	—	—
"	30	—	—
Feb.	4	—	—

Post-mortem examination (one hour after death). Animal very anæmic and wasted. Blood-film shows no trypanosomes. Organs pale, but not unhealthy. Intestine contains a large tape-worm. Trypanosomes not present in the cerebro-spinal fluid. Brain appears normal.

EXPERIMENT 341. MONKEY. MALE. (*Cercopithecus sp.*) WEIGHT 3·5 KILOS.

December 7, 1904. Injected arsenic, 5 milligrammes, equal to 1 milligramme of arsenic per 700 grammes monkey, and just half the maximum dose.

December 9. Inject 2 cubic centimetres of blood from Kitsame (an early case of trypanosome infection).

December 23. Trypanosomes appeared in the blood to-day.

December 27. Trypanosomes numerous in blood. Inject arsenic, 7 milligrammes.

January 13. Trypanosomes again present in the blood, having been absent for the last 17 days.

January 14. Inject arsenic 8 milligrammes.

February 4. Animal died to-day. Trypanosomes have been absent from the blood since the last injection of arsenic.

The following table shows the presence or absence of trypanosomes in the blood :—

Date.	Parasites in Blood.			Parasites in Cerebro-spinal Fluid.		As ₂ O ₃ in milligrammes.			
	Fil.	Mal.	Tryp.	Strept.	Tryp.				
1904.									
Dec. 16	—	+	—
" 23	—	+	+
" 27	—	+	+
" 29	—	+	—	7
" 31	—	+	—
1905.									
Jan. 5	—	+	—
" 13	—	+	+
" 14	—	+	+
" 17	—	+	—	8
" 21	—	+	—
" 23	—	+	—
" 29	—	+	—
Feb. 4	—	+	—	—	—	...

Post-mortem examination. Heart, normal; lungs, very pale; a few scattered petechiæ in the pleuræ. Stomach shows no ulceration, but a few flecks of altered blood here and there. Liver has an abscess, the size of two walnuts, at the lower border of the liver substance. Contents consist of thick yellow curdy pus. A smear shows the presence of a large *Diplococcus*. Kidneys, normal. Lymphatic glands not enlarged. Brain appears quite normal. Trypanosomes appeared in the blood of this animal fourteen days after inoculation, in spite of the large dose of arsenic which had been given 36 hours before.

EXPERIMENT 350. MONKEY (*Cercopithecus sp.*). CONTROL.

December 21, 1904. Blood examined. Trypanosomes are absent. Injected subcutaneously 3 cubic centimetres of cerebro-spinal fluid from sleeping sickness case (Abyabu), containing numerous trypanosomes.

January 13. Trypanosomes appeared in the blood to-day for the first time.

March 8. Animal is getting thin. Trypanosomes have been continuously present in the blood.

April 4. Animal died to-day.

The following table shows the presence or absence of trypanosomes in the blood :—

Date.				Parasites in Blood.		Parasites in Cerebro-spinal fluid.		As ₂ O ₃ milligrammes.	
				Mal.	Tryp.	Strept.	Tryp.		
1904.									
Dec.	19...	+	—	None.	
"	21...	Inoculated with trypanosomes.					
"	30...	+	—		
1905.									
Jan.	5...	+	—		
"	13...	+	+		
"	23...	+	+		
"	30...	+	+		
Feb.	5...	+	+		
"	13...	+	+		
"	21...	+	+		
March	1...	+	+		
"	8	+	+		
"	17...	+	+		
"	28...	+	+		
April	4...	+	+		

Post-mortem examination (one hour after death). Animal thin and anæmic. Blood-film contains trypanosomes in large numbers. No superficial glandular enlargement. Brain appears normal. Specimen of cerebro-spinal fluid contains a little blood ; trypanosomes are present in it, but not in very large numbers. Stomach.—A few minute points of superficial ulceration are scattered over the mucous membrane. Each ulcer is covered with a point of blood clot. All other viscera normal.

(2) *Trypanroth* (Ehrlich).

We have injected several fresh monkeys with a solution of trypanroth with a view to ascertaining how much of this drug can be safely given to these animals. Unfortunately, many of our monkeys so injected developed large abscesses at the seat of injection, and in some cases died from the effects of such abscesses. Monkeys injected in this way became deeply pigmented all over, the pigmentation getting to its full depth in 48 hours.

TABLE VIII.

To show the effects of different doses of Trypanroth on Monkeys.

Letter of Animal.	Weight of Animal.	Trypanroth, 2 per cent. solution.	Trypanroth per weight of Monkey.	Result.
A.	3.64 kilos.	25 cubic centimetres.	1 milligramme per 7.5 grammes monkey.	Died.
B.	1.36 „	7 cubic centimetres.	1 milligramme per 10 grammes monkey.	Fatal in 12 days. Abscess formed.
C.	1.8 „	9 cubic centimetres.	1 milligramme per 10 grammes monkey.	Fatal in 7 days from abscess.
D.	1.25 „	5 cubic centimetres.	1 milligramme per 12.5 grammes monkey.	Died a month later for no apparent reason.

From these experiments it seems that 1 milligramme of trypanroth per 12 grammes monkey is about the minimum lethal dose.

We give the account of an experiment in which a monkey suffering from the trypanosome of sleeping sickness was unsuccessfully treated with a solution of trypanroth. The trypanosomes disappeared for a time but returned to the circulation in 12 days.

EXPERIMENT 314. MONKEY (*Cercopithecus* sp.).

WEIGHT 1.786 KILOGRAMMES.

August 15. Blood examined; trypanosomes absent. Inject 5 cubic centimetres of blood, containing numerous trypanosomes, from sleeping sickness case (Abyabu).

August 26. Trypanosomes have appeared in the blood to-day for the first time, 11 days after inoculation.

October 26. For the last two months, trypanosomes have been continually present in the animal's blood. Inject subcutaneously 10 cubic centimetres of 1 per cent. solution of trypanroth (*i.e.* 1 milligramme trypanroth per 17.8 grammes monkey).

October 28. Animal's skin has a deep red colour. Site of inoculation appears healthy. Trypanosomes absent from blood.

November 2. Animal seems none the worse for the drug. Trypanosomes are still absent from the blood.

November 7. Trypanosomes have reappeared in the blood again to-day. Animal's skin is still of a deep red colour.

December 19.—Trypanosomes have been constantly present in the blood since November 7. Inject 5 milligrammes arsenic (*i.e.* 1 milligramme per 160 grammes monkey). This dose proved fatal to the monkey.

VI. *On the Identity of the Trypanosome of Sleeping Sickness with Trypanosoma Gambiense;*

An account of Inoculation Experiments on 32 Rats and on a Chimpanzee.

Following the suggestion of the Tropical Diseases Committee of the Royal Society, that there might be more than one species of human trypanosome in Uganda, we have inoculated white

rats with human trypanosomes from as many sources as possible. White rats were used because of the recent announcement by Mr. Plimmer, that these animals react very differently to *Trypanosoma gambiense* on the one hand and to the trypanosome of Uganda sleeping sickness on the other, the author reporting that white rats inoculated with the former trypanosome die in a little more than two months, with swarms of parasites in their peripheral blood, while those infected with the latter parasite die with paralysis of the hind limbs, and with parasites only to be found in the spinal cord, six to nine months after inoculation.

The rats used by us have all been bred out in Entebbe from parents sent to us from England. They were not used for inoculation experiments until they were at least four months old. Our stock of uninoculated rats has always been very healthy; we have not lost a single uninfected animal from intercurrent disease. All rats inoculated with different strains of human trypanosome have been kept apart in separate cages, and each rat has been identified by its sex, &c., and by cuts or other marks in one or both ears.

We have inoculated rats from the following sources :—

- A. *The cerebro-spinal fluid of sleeping sickness patients.*
- B. *The blood of monkeys infected from the cerebro-spinal fluid of sleeping sickness patients.*
- C. *The blood of sleeping sickness patients.*
- D. *The blood of patients with trypanosomiasis, but with no symptoms of sleeping sickness.*
- E. *The blood of monkeys infected from the blood of trypanosomiasis patients, with no symptoms of sleeping sickness.*
- F. *The gland-juice of patients with sleeping sickness.*
- G. *The gland-juice of patients with trypanosomiasis, but with no symptoms of sleeping sickness.*

Of 32 rats inoculated with trypanosomes from these seven sources, all but 13 have shown trypanosomes in their peripheral blood since inoculation. Four of these 13 may yet do so, as it is only a few weeks since they were inoculated.

Class A.—Of six rats inoculated, only two have shown trypanosomes in their peripheral blood. In these two rats the parasites have always been very scanty. All the rats remain healthy.

Class B.—Consisted originally of four rats all inoculated with blood from a monkey infected with cerebro-spinal fluid from a typical case of sleeping sickness. The blood used to inoculate them was taken from the monkey two months after it had been infected with the cerebro-spinal fluid. The blood was moderately rich in trypanosomes at the time. Trypanosomes appeared in the blood of these four rats ten or eleven days after inoculation, to reappear at intervals and in very scanty numbers up to the time of death. All these rats showed paralysis of their hind limbs for ten or more days before their death, which occurred from

three to four months after inoculation. In three out of the four animals, trypanosomes could not be found in the peripheral blood at the time of death. In the fourth, trypanosomes were present in very scanty numbers.

When examined after death, trypanosomes were found to be present in the brains and spinal cords of these four rats in considerable numbers. Sections of these brains and spinal cords, stained by Leishman's special method, showed trypanosomes scattered all through the nervous matter, apparently more numerous in the brain than in the spinal cord. Trypanosomes could not be seen in the brain capillaries. The sections of all four brains showed small-celled infiltration around the blood vessels in the brain-substance, the typical lesion of sleeping sickness.

Other rats inoculated with trypanosomes from these paralysed rats have shown trypanosomes in their blood in much greater numbers and far oftener than was the case with the original rats. One of these rats so inoculated has already died, and is worthy of notice. Trypanosomes appeared in its blood 33 days after inoculation with a few drops of spinal-cord emulsion, taken *post-mortem* from one of the paralysed rats. Trypanosomes became more and more numerous in this animal's blood until death occurred just two-and-a-half months from the time of inoculation. At death the spleen was enormously large, the liver was considerably enlarged and the blood swarmed with parasites. This rat never showed any signs of paralysis.

Class C.—Four rats have been inoculated with blood from sleeping sickness patients in the last stage of the disease, but trypanosomes have not appeared in their blood up to now.

Class D.—Four rats were inoculated from the blood of an Indian, who simply showed fever and trypanosomes in his blood, in July, 1905. Only one of these rats has ever shown trypanosomes in its blood since inoculation. For six-and-a-half months this rat remained in good health, showing trypanosomes in its blood at rare intervals. It then developed paralysis of the hind limbs, and died on March 1, 1906, with numerous trypanosomes in the brain and spinal cord.

Class E.—A single rat in this class shows scanty parasites in its blood. It remains in good health.

Class F.—Two rats inoculated with the gland-juice of advanced cases of sleeping sickness have not yet shown trypanosomes in their peripheral blood. Both these rats remain healthy.

Class G.—Two rats inoculated with the gland-juice taken from very early cases of trypanosome-infection show trypanosomes in their blood at rare intervals, and at present remain healthy.

It is evident that, on examining the history of the rats in class B, one and the same strain of trypanosome, obtained

originally from a case of sleeping sickness (cerebro-spinal fluid), has produced death in similar animals in two distinct and very different ways. The mode of death in the first four rats corresponds to that accredited by Plimmer to the trypanosome of Uganda sleeping sickness. The disease, death and *post-mortem* appearances in the other rats inoculated from one of the above, are identical with what have often been described for rats inoculated with the trypanosome of Gambia fever. So the same strain of trypanosome has in this way been made to produce the two different effects which were brought forward in support of the theory that the parasite of Gambia fever was distinct from that of Uganda sleeping sickness. It seems also that rats inoculated with trypanosomes from the spinal-fluid of sleeping sickness cases as well as rats inoculated with blood from cases of *Trypanosoma* fever may both die with marked symptoms of paralysis.

From these experiments we infer that there is only one variety of human trypanosome in Uganda, and that it is identical with *Trypanosoma gambiense*.

The following table gives an outline of our experiments on these white rats, and after it we describe a few of the more interesting experiments in detail:—

TABLE IX.

Class A.

Rats Inoculated with Cerebro-spinal Fluid from Sleeping Sickness cases.

Number of Experiment.	Date of Inoculation.	Date of appearance in Peripheral Blood.	Number of Parasites usually seen.	Result. Date of Death.
449	1905. July 14	Never shown parasites.		Alive and well, March, 1906.
450*	" 14	1905. Aug. 2 ... (19 days.)	Only shown on three occasions, very scantily.	Alive and well, March, 1906.
479	Sept. 14	Oct. 21 ... (37 days.)	Shown twice, very scanty.	Alive and well, March, 1906.
480	" 14	Never shown parasites.		Died on Dec. 1, 1905, in giving birth.
541	Dec. 6	Not yet shown parasites.		Alive and well, March, 1906.
542	" 6	" " "		Alive and well, March, 1906.

* In these tables case marked with an asterisk are subsequently given in fuller detail.

Class B.

Rats Inoculated with Blood from Monkeys, which had been previously Inoculated with Cerebro-spinal Fluid from Sleeping Sickness Patients.

Number of Experiment.	Date of Inoculation.	Date of appearance in Peripheral Blood.	Number of Parasites usually seen.	Result. Date of Death.
FIRST PASSAGE.				
451	1905. July 17	1905. July 28 ... (11 days.)	Shown several times; parasites always scanty.	Died Nov. 6, 1905, with paralysis.
452	" 17	July 27 ... (10 days.)	Shown several times; parasites always scanty.	Died Oct. 19, 1905, with paralysis.
453 (a)	" 17	July 27 ... (10 days.)	Shown several times; parasites always scanty.	Died Nov. 6, 1905, with paralysis.
453 (b)*	" 17	July 27 ... (10 days.)	Shown several times; parasites always scanty.	Died Oct. 26 1905, with paralysis.
509	Oct. 20	Nov. 28 ... (39 days.)	Shown parasites once only.	Alive and well, March, 1906.
SECOND PASSAGE.				
512* (From 453 (b) above.)	Oct. 26	Nov. 7 ... (12 days.)	Parasites generally present, often numerous.	Alive and well, March, 1906.
513* (From 453 (b) above.)	" 26	Nov. 28 ... (33 days.)	Parasites very numerous, increasing till death.	Died Jan. 8, 1906. No paralysis, large spleen, bloodswarming with trypanosomes.
514 ³ (From 453 (b).)	" 26	Nov. 22 ... (27 days.)	Often numerous.	Alive and well, March, 1906.
519 (From 453 (a).)	Nov. 6	Nov. 22 ... (16 days.)	Often numerous.	Alive and well, March, 1906.
520 (From 453 (a).)	" 6	Nov. 16 ... (10 days.)	Generally scanty.	Alive and well, March, 1906.
THIRD PASSAGE.				
526 (From 514.)	Nov. 29	Dec. 12 ... (13 days.)	Moderate numbers.	Alive and well, March, 1906.
527 (From 514.)	" 29	1906. Jan. 9 ... (41 days.)	Scanty numbers.	Alive and well, March, 1906.
546. (From 513.)	Dec. 28	Jan. 2 ... (5 days.)	Rather scanty at present.	Alive and well, March, 1906.

* In these tables case marked with an asterisk are subsequently given in fuller detail.

Class C.

Rats Inoculated with Blood taken from Sleeping Sickness Patients, and containing Trypanosomes in moderate numbers.

No. of Experiment	Date of Inoculation.	Date of appearance in Peripheral Blood.	Number of Parasites usually seen.	Result.
516	1905. Oct. 30	Never shown parasites		Alive and well, March, 1906.
517	" 30	" "	"	Alive and well, March, 1906.
543	Dec. 7	Not yet shown parasites		Alive and well, March, 1906.
544	" 7	" "	"	Alive and well, March, 1906.

Class D.

Rats Inoculated from Patients showing Trypanosomes in their Peripheral Blood, but with no symptoms of Sleeping Sickness.

No. of Experiment.	Date of Inoculation.	Date of appearance in Peripheral Blood.	Number of Parasites usually seen.	Result. Date of Death.
455	1905. July 17	Never shown parasites		Alive and well, March, 1906.
456	" 17	" "	"	Alive and well, March, 1906.
457	" 17	" "	"	Alive and well, March, 1906.
458 [*]	" 17	1905. Aug. 12 ... (26 days.)	Showed for a month in moderate numbers; not shown for three months.	Developed paralysis of hind limbs in Jan., 1906, and died on March 1, 1906.

^{*} In these tables cases marked with an asterisk are subsequently given in fuller detail.

Class E.

Rat Inoculated with Blood from Monkey infected with Blood from Patient showing no signs of Sleeping Sickness, but whose Blood contained Trypanosomes.

No. of Experiment.	Date of Inoculation.	Date of appearance in Peripheral Blood.	Number of Parasites usually seen.	Result.
545	1905. Dec. 12	1906. Jan. 3 ... (22 days.)	Scanty at present.	Alive and well, March, 1906.

Class F.

Rats inoculated with Gland-Juice from Patients suffering from Sleeping Sickness.

No of Experiment.	Date of Inoculation.	Date of appearance in Peripheral Blood.	Number of Parasites usually seen.	Result.
508	1905. Oct. 20	Never shown parasites		Alive and well, March, 1906.
523	Nov. 15			Alive and well, March, 1906.

Class G.

Rats Inoculated with Gland-Juice from Patients with Trypanosomiasis, but who show no signs of Sleeping Sickness.

No. of Experiment.	Date of Inoculation.	Date of appearance in Peripheral Blood.	Number of Parasites usually seen.	Result.
503	1905. Oct. 10	1905. Nov. 1 ... (22 days.)	Only shown once, in very scanty numbers. Shown twice, very scantily.	Alive and well, March, 1906.
521	Nov. 13	Nov. 22 ... (9 days.)		Alive and well, March, 1906.

Details of some of the Experiments shown in the foregoing tables :—

Class A.

No. 450. RAT (WHITE). MALE. RIGHT EAR CUT.

July 14, 1905. Inject subcutaneously the deposit from 10 cubic centimetres of cerebro-spinal fluid left after centrifuging, taken from a case of well-marked sleeping sickness. Trypanosomes are present in this deposit in moderate numbers.

August 2. Trypanosomes have appeared in the blood to-day in scanty numbers.

October 4. Animal remains in good health. Trypanosomes are not to be found in the blood.

November 1. Trypanosomes again present in the blood in very scanty numbers.

January 9, 1906. Animal remains in apparently perfect health.

The following table shows the result of the blood examinations :—

Date.	Trypano- somes.	Date.	Trypano- somes.	Date.	Trypano- somes.
1905:		1905.		1905.	
July 14 ...	—	Aug. 14 ...	—	Nov. 1 ...	+
" 21 ...	—	" 16 ...	—	" 12 ...	—
" 23 ...	—	" 19 ...	—	" 16 ...	—
" 25 ...	—	" 22 ...	+	" 22 ...	—
" 27 ...	—	" 27 ...	—	" 28 ...	—
" 29 ...	—	Sept. 1 ...	—	Dec. 5 ...	—
" 31 ...	—	" 6 ...	—	" 12 ...	—
Aug. 2 ...	+	" 13 ...	—	" 20 ...	—
" 4 ...	—	" 20 ...	—	" 27 ...	—
" 6 ...	—	" 27 ...	—		
" 8 ...	—	Oct. 4 ...	—	1906.	
" 10 ...	—	" 19 ...	—	Jan. 3 ...	—
" 12 ...	—	" 25 ...	—	" 9 ...	—

Class B.

No. 453 (b). RAT (WHITE). FEMALE. RIGHT EAR NOTCHED.

July 17, 1905. Inject subcutaneously three drops of blood and citrate solution from monkey 420.

July 27. Trypanosomes scantily present in the blood to-day.

October 19. There is well-marked paralysis of the hind limbs. Otherwise animal seems fairly well. Trypanosomes have not been found in the blood since Sept. 6.

October 23. Animal is getting thin and seems very sick. Extreme paralysis of hind limbs.

October 26. Animal moribund, and killed.

The following table shows the presence or absence of trypanosomes in the blood :—

Date.	Trypano- somes.	Date.	Trypano- somes.	Date.	Trypano- somes.
1905.		1905.		1905.	
July 21 ...	—	Aug. 19 ...	+	Sept. 27 ...	—
" 23 ...	—	" 23 ...	—	Oct. 4 ...	—
" 25 ...	—	" 27 ...	—	" 11 ...	—
" 27 ...	+	Sept. 1 ...	—	" 19 ...	—
Aug. 4 ...	—	" 6 ...	+	" 20 ...	—
" 8 ...	+	" 13 ...	—	" 25 ...	—
" 16 ...	—	" 20 ...	—	" 26 ...	—

October 26. *Post-mortem* examination, immediately after death. The animal is decidedly thin. No oedema of the body wall. Eyes normal. No enlargement of the superficial lymphatic glands. The coat is rough and full of lice. All the viscera of the thorax and abdomen appear quite healthy. Spleen a little larger than normal. Brain and spinal cord appear normal to the naked eye. Trypanosomes not present in a blood-film. Emulsions in normal citrate solution were then made of the brain, spinal cord and thoracic and abdominal viscera. These emulsions having been centrifuged, the deposits were examined. Trypanosomes were found to be numerous in the brain, to be present in moderate numbers in the spinal cord and to be scanty in the other viscera. Other rats were inoculated with portions of these emulsions. Sections of the brain and spinal cord, stained by Leishman's method, showed well-marked small-celled infiltration around the cerebral blood-vessels. Numerous trypanosomes could be seen scattered all through the brain-substance.

Class B.

SECOND PASSAGE.

NO. 513. RAT (BLACK AND WHITE). MALE. BOTH EARS CUT.

October 26, 1905. Inject subcutaneously a few drops of an emulsion in normal citrate of the spinal cord of rat 453 (*b*).

November 28. Trypanosomes have appeared in the animal's blood to-day.

December 27. Trypanosomes have now become numerous in this animal's blood. Animal seems in good health.

January 4, 1906. Trypanosomes have now become about half as numerous in the blood as the red corpuscles. A few nucleated red corpuscles are present.

January 8. Animal died. Trypanosomes swarmed in the blood just before death, and were as numerous as the red corpuscles.

The following table shows the result of the blood examinations :—

Date.	Trypano- somes.	Date.	Trypano- somes.	Date.	Trypano- somes.
1905.		1905.		1906.	
Oct. 26 ...	—	Dec. 28 ...	+ +	Jan. 2 ...	+ +
Nov. 7 ...	—	" 29 ...	+ +	" 3 ...	+ +
" 22 ...	—	" 30 ...	+ +	" 4 ...	+ +
" 28 ...	+	" 31 ...	+ +	" 5 ...	+ +
Dec. 5 ...	+			" 6 ...	+ +
" 12 ...	+	1906.		" 7 ...	+ + +
" 20 ...	+	Jan. 1 ...	+ +	" 8 ...	+ + +
" 27 ...	+ +				

January 8. A *post-mortem* examination was made at death. Animal is thin, but not emaciated. Trypanosomes very numerous in the peripheral blood. Superficial lymphatic glands enlarged. Abdominal and mesenteric glands enlarged. Lungs and heart appear normal. Spleen enormously enlarged. Weight 4.35 grammes. Length 6.5 centimetres. Breadth 1.3 centimetres. Liver considerably enlarged; weight 12 grammes. Kidneys appear normal. Urine in bladder normal. Brain and spinal cord appear normal. Smears of the brain, when a brain capillary is seen in the smear, show the capillary swarming with trypanosomes. Smears of spleen show trypanosomes in very large numbers.

NO. 512. RAT (BLACK AND WHITE). FEMALE. TWO CUTS IN EACH EAR.

October 26, 1905. Inject subcutaneously a few drops of an emulsion in normal citrate of the brain of rat 453 (b).

November 7. Trypanosomes have appeared in the blood to-day.

January 8, 1906. Trypanosomes have several times been numerous in the blood. Animal is apparently in good health. There are no symptoms of paralysis.

The following table shows the result of the blood examinations :—

Date.	Trypano- somes.	Date.	Trypano- somes.	Date.	Trypano- somes.
1905.		1905.		1906.	
Oct. 26 ...	—	Dec. 12 ...	—	Jan. 2 ...	+
Nov. 7 ...	+	" 20 ...	+	" 3 ...	+
" 12 ...	+	" 27 ...	—	" 4 ...	+
" 22 ...	—	" 29 ...	+	" 5 ...	+
" 28 ...	+	" 30 ...	—	" 7 ...	—
Dec. 5 ...	—	" 31 ...	—	" 8 ...	+

NO. 514. RAT (WHITE). FEMALE.

October 26, 1905. Inject subcutaneously a few drops of the deposit left after centrifuging the blood, and emulsified viscera of rat 453 (b).

November 22. Trypanosomes have appeared in the blood to-day.

November 28. Trypanosomes have now become very numerous in the blood. Animal seems in good health.

November 30. Trypanosomes have become comparatively scanty in the blood.

January 8, 1906. Animal remains in good health. No symptoms of paralysis. Trypanosomes remain present in the blood in scanty numbers.

The following table shows the result of the blood examinations :—

Date.	Trypano- somes.	Date.	Trypano- somes.	Date.	Trypano- somes.
1905.		1905.		1906.	
Oct. 26 ...	—	Dec. 2 ...	+	Jan. 1 ...	—
Nov. 7 ...	—	" 5 ...	+	" 2 ...	+
" 16 ...	—	" 12 ...	+	" 3 ...	+
" 22 ...	+	" 20 ...	—	" 6 ...	+
" 28 ...	++	" 27 ...	+	" 8 ...	+
" 29 ...	++	" 29 ...	—	" 9 ...	+
" 30 ...	+				

Class D.

NO. 458. RAT (BLACK AND WHITE). FEMALE. RIGHT EAR CUT.

July 17, 1905. Inject subcutaneously a few drops of blood, mixed with normal citrate, taken from Ladha Singh, a sepoy, whose blood contains trypanosomes in moderate numbers.

August 12. Trypanosomes have appeared in the animal's blood to-day in scanty numbers.

September 13. Trypanosomes have been present in the blood continuously for the last month. The parasites have always been quite scanty. Animal remains in good health.

January 9, 1906. Animal remains in good health. Trypanosomes have not been present in the blood since the middle of September.

The following table shows the result of the blood examinations :—

Date.	Trypano- somes.	Date.	Trypano- somes.	Date.	Trypano- somes.
1905.		1905.		1905.	
July 17 ...	—	Aug. 16 ...	+	Nov. 12 ...	—
" 21 ...	—	" 19 ...	+	" 16 ...	—
" 23 ...	—	" 23 ...	—	" 22 ...	—
" 25 ...	—	" 27 ...	+	" 28 ...	—
" 27 ...	—	Sept. 1 ...	+	Dec. 5 ...	—
" 29 ...	—	" 6 ...	+	" 12 ...	—
" 31 ...	—	" 13 ...	+	" 20 ...	—
Aug. 2 ...	—	" 20 ...	—	" 27 ...	—
" 4 ...	—	" 27 ...	—		
" 6 ...	—	Oct. 4 ...	—	1906.	
" 8 ...	—	" 19 ...	—	Jan. 3 ...	—
" 12 ...	+	Nov. 1 ..	—	" 9 ...	—
" 14 ...	+				

January 23. This rat has now developed paralysis of the hind limbs. Trypanosomes are not present in the blood.

No. 394. CHIMPANZEE.

March 1, 1905. Examine animal's blood. Trypanosomes are absent. Animal seems healthy. Glands not palpable. Remove 30 cubic centimetres of cerebro-spinal fluid from Zenabu (a well marked case of sleeping sickness), and inject it subcutaneously into the left fore-arm of the chimpanzee. An examination of a further 8 cubic centimetres of cerebro-spinal fluid show that trypanosomes are present in it in scanty numbers. The fluid was quite free from blood, and was sterile on cultivation.

March 18. Trypanosomes are present in the animal's blood to-day. They are normal in appearance and numerous. Animal still very savage.

April 7. Animal's condition remains unaltered. Temperature 101°. Still takes his food well. Trypanosomes numerous in the blood.

May 1. Temperature 102°. Animal is suffering from tape-worm. Blood contains a few nucleated red cells. Trypanosomes are present but scanty.

May 15. Condition remains good, but animal is slightly thinner than on arrival. There is some fulness under the eyes. No enlarged glands can be felt.

May 29. Animal sits a great deal with his hands to his head. Coat is looking ragged. Trypanosomes are present in the blood, but in very scanty numbers.

June 12. Temperature 103°. Trypanosomes are absent from the blood. A distinct fulness under the eyes.

June 24. Enlarged glands felt in the right axilla. Gland punctured; gland-juice contains actively motile trypanosomes in fair numbers. Trypanosomes are absent from the blood.

July 6. Animal is much weaker than formerly; trypanosomes are present in the gland-juice but cannot be found in a blood-film.

July 22. Animal very thin and sick. Appetite bad. Temperature 95°. Gland-juice contains numerous trypanosomes. Blood-film negative.

July 29. Animal is getting worse every day. Temperature 95°·4. There is no tremor. Marked emaciation.

August 8. Animal died to-day.

Post-mortem examination one hour after death. Body is very thin and wasted. There is marked general superficial glandular enlargement. Smears of the gland-juice show trypanosomes in scanty numbers.

Trypanosomes not present in the cerebro-spinal fluid. Surface of brain normal, no thickening of the membranes. Brain appears normal to the naked eye. Smears of brain-substance showed nothing noteworthy. Sections of (1) cortex, (2) basal ganglia, (3) pons, and (4) medulla, were made and examined, but showed none of the changes characteristic of death from sleeping sickness in men.

Lungs and heart, normal. Liver, large and fatty. Kidneys, pale and somewhat soft. Capsule strips normally. Spleen, normal; weighs 4 ozs. Stomach, dilated; surface of mucous membrane pale, but otherwise normal. Blood-films taken and examined after death, do not show the presence of trypanosomes. Smears of the gland-juice taken from the cervical and axillary glands after death are also negative.

The following table shows the results of the blood and gland examinations, &c.

Date:				Percentages:					Parasites in Glands.		Parasites in Blood.			In Cerebro-spinal Fluid.	
				Poly.	Small.	Large.	Tos.	Bas.	Strept.	Tryp.	Fil.	Mal.	Tryp.	Strept.	Tryp.
March	1	—	—	—
"	18	37	50	8	5	+	—	+
April	7	—	—	+
May	1	36	50	11	3	+	—	+
"	15	62	27	11	—	+	—	+
"	29	59	37	4	—	+	—	+
June	12	—	—	—
"	24	53	41	3	—	+	—	—
July	5	55	42	3	—	+	—	—	—
"	12	33	60	7	—	+	+	—	—
"	22	+	+	—	—
"	29	+	+	—	—
Aug.	8	—	—	—	...	—

Unfortunately this animal died from the effects of captivity six months after inoculation. It is interesting to note, however, that enlargement of the lymphatic glands appeared three months after inoculation, and that trypanosomes could easily be found in the gland-juice when prolonged examination of blood-films proved negative.

VII.—On the occurrence of *Trypanosoma Gambiense* in the Blood of Native Dogs in Uganda.

In Report No. VI., p. 275, where mention was made of an outbreak of sleeping sickness at Bugungu, at the north eastern extremity of the Albert Nyanza, it was also stated that the dogs of that district were said to be suffering from some wasting disease and that trypanosomes had been found in one of

these animals. Dr. Pooley, the medical officer of the district, kindly obtained two of these native dogs for us, and had them forwarded to Entebbe, where they arrived on November 28, 1904. Both of them then presented a similar appearance. They were decidedly thin, their coats were rough and dirty and full of fleas. One of them showed some slight glandular enlargement in the axilla. There was no œdema or swelling of any part of their bodies. The ears of both animals were ragged and covered with scabs. Both dogs could run and walk normally and devoured their food eagerly. Their eyes were normal.

EXPERIMENT NO. 332. DOG (NATIVE). MALE.

November 28, 1904. Blood examined; trypanosomes absent, no other parasite seen; temperature 102°.

December 13. Blood again examined, nothing found. Animal very anæmic, and getting thinner. Segments of tape-worm found in motions.

January 5, 1905. Trypanosomes found in blood to-day in moderate numbers. This trypanosome in size and shape is practically identical with that of sleeping sickness in the blood of human beings.

January 12. Animal now very weak and ill and does not eat his food well. Trypanosomes cannot be found in the blood to-day.

January 17. Trypanosomes again present in the blood. There is no œdema or swelling in any part of the body. Eyes normal. Animal is extremely anæmic.

January 25. Animal died to-day.

The following tables shows the result of the blood examinations:—

Date.	Parasites in Blood.	Parasites in Cerebro- spinal Fluid.	Date.	Parasites in Blood.	Parasites in Cerebro- spinal Fluid.
	Trypano- somes.	Trypano- somes.		Trypano- somes.	Trypano- somes.
1904.			1905.		
Nov. 28 ...	—	...	Jan. 9 ...	—	...
Dec. 6 ...	—	...	" 10 ...	—	...
" 13 ...	—	...	" 14 ...	—	...
			" 17 ...	+	...
1905.			" 24 ...	+	—
Jan. 5 ...	+	...			

Post-mortem examination (immediately after death). The body is extremely emaciated, abdomen retracted, whole carcass is covered with fleas and there are many ticks on the ears. Mucous membranes very anæmic. Eyes normal. No œdema. Lymphatic glands in axillæ and groin slightly enlarged, but not abnormal on section. Subcutaneous tissue normal.

On opening abdomen and thorax, both cavities are found to be free of fluid. Pericardium is normal. Heart, very anæmic, otherwise normal. Lungs, healthy. Spleen, not enlarged, normal on section. Kidneys, capsules strip off readily, very pale. Stomach and intestines show many small, white, thread-like worms in stomach and duodenum—*Ankylostoma*. Intestines are swarming with *Tenia solium*; mucous membrane very pale.

Death was probably due to ankylostomiasis in this animal. Trypanosomes were only found occasionally in the blood, and never in large numbers.

EXPERIMENT NO. 333. DOG (NATIVE). MALE.

November 28, 1904. Blood examined, nothing abnormal found.

January 5, 1905. Animal intensely anæmic and emaciated. Eyes normal. No œdema or swelling of any part of the body. Animal can still walk and even run when urged.

January 15. Trypanosomes found in the blood to-day for the first time in scanty numbers. The parasite exactly resembles that found in a dog (Experiment No. 332) about ten days ago.

January 24. Animal died to-day. He has been getting steadily thinner and weaker, but there have been no other symptoms. For the last two days he has refused his food.

The following table gives the result of the blood examinations:—

Date:	Parasites in Blood.		Parasites in Cerebro-spinal Fluid.	Date.	Parasites in Blood.		Parasites in Cerebro-spinal Fluid.
	Pyro-somes.	Trypano-somes.	Trypano-somes.		Pyro-somes.	Trypano-somes.	Trypano-somes.
1904.				1905.			
Nov. 28	—	—	...	Jan. 10	—	—	...
Dec. 6	—	—	...	" 15	—	+	...
" 13	—	—	...	" 20	—	—	...
				" 24	—	+	—
1905.							
Jan. 5	—	—	...				

Post-mortem examination made a few minutes after death. A blood-film contains trypanosomes in moderate numbers. Emaciation very marked. Eyes normal. No swelling or œdema of any part of the body. Lymphatic glands not enlarged. Subcutaneous tissue normal. Pericardium, normal. Heart, very pale. Cavities somewhat dilated. Lungs show a few small areas of collapse, very pale. Spleen not enlarged, normal on section. Kidneys, normal. Stomach and intestines swarming with worms. Ankylostoma and *Tenia solium*. Brain showed nothing abnormal.

Death in this animal was almost certainly due to anæmia from the swarms of Ankylostoma present.

Evidence that the trypanosome found in the native Dogs from Bugungu is identical with the Trypanosoma Gambiense of Sleeping Sickness.

The trypanosome found in the two dogs sent to us from Bugungu is morphologically indistinguishable from the human parasite of sleeping sickness. In the original dogs sent to us the disease must have lasted at least three months, if, as it is only reasonable to suppose, these animals were already infected when they started on their journey to Entebbe. These two dogs presented none of the recognised symptoms of Nagana, such as swelling and œdema of the extremities, opacity of the cornea, or skin-eruption. At their death, rather more than three months after leaving Bugungu, they were thin, anæmic, and swarming with intestinal worms. While they were at Entebbe, trypanosomes could only rarely be found in a drop of their blood. On examining the animals after death, trypanosomes were

numerous in the blood of both of them, but with no gland-enlargement, subcutaneous infiltration, or jelly-like deposit on the pericardium. In neither case was the spleen enlarged.

Injection experiments with this trypanosome on other animals have given the following results :—

A donkey, a bullock, and two goats have never shown trypanosomes in their blood since their inoculation six months ago. These animals are still apparently in good health.

A dog inoculated in July, 1905, died at the end of January, 1906 ; seven months after infection trypanosomes were always present in his blood, generally in considerable numbers.

Two cats inoculated in July are also alive and apparently healthy, although their blood constantly shows the presence of parasites. Two monkeys lived four and five months respectively after infection with this trypanosome. Their blood generally showed the presence of the parasite.

Two out of the three guinea-pigs inoculated with this trypanosome showed the parasite 19 days afterwards. One animal, which lived nine months, always showed the parasite in considerable numbers in its blood. The other animal died on its way to England. Of four rats inoculated with this parasite, one has died with paralysis of the hind limbs, and with trypanosomes numerous in the brain and spinal cord, but scanty in the blood, four months after infection. The other three rats have all quite occasionally shown the parasite in their blood. They seem at present in good health.

From these experiments it may be inferred that the trypanosome found in the dogs sent to us from Bugungu is really the trypanosome of sleeping sickness. This disease, at the time when these dogs were sent to us, had already broken out at Bugungu, and now, after a year's interval, has there assumed serious proportions. That the tsetse fly bites dogs is a fact well known to anyone who has taken a dog into a fly-infested area. Whether dogs infected with the trypanosome of sleeping sickness actually die from such infection does not at present seem clear. The two original dogs from Bugungu certainly died in our laboratory within a few days of one another, but they were very anæmic from swarms of intestinal parasites (*Ankylostoma*, *Tænia*, &c.). A healthy dog inoculated from one of them has just died, seven months after infection ; trypanosomes were constantly present in his blood. Dogs inoculated with the trypanosome of sleeping sickness by former members of this Commission, and kept in this laboratory, all died of ankylostomiasis, and in no single case was death attributed to their trypanosomes.

It seems then, that in areas of sleeping sickness dogs as well as men may act as carriers of the disease. The fact that infected dogs may live a long while, and, as a rule, show the parasite in their peripheral blood in far greater numbers than is the case with human beings, makes them of considerable importance as a source of infection in districts infested with flies.

Good May/09

As the question of the identity of this "Bugungu" trypanosome with *Trypanosoma gambiense* appears to us to be of considerable importance, we give in detail the results of inoculation experiments performed by us with it.

EXPERIMENT NO. 209 (a). OX (FAWN).

January 24, 1905. Injected subcutaneously 10 cubic centimetres of blood from dog, Experiment No. 333, containing trypanosomes in moderate numbers.

April 27. This animal's blood has been regularly examined every week up to now, but trypanosomes have never been found in it. The animal remains in good health.

August 1. Animal still in good health. Trypanosomes have never appeared in its blood.

EXPERIMENT NO. 296 (a). GOAT (BLACK AND WHITE).

January 25, 1905. Injected subcutaneously 5 cubic centimetres of blood from dog Experiment No. 332, containing trypanosomes in scanty numbers.

April 27. Animal remains in good health. Its blood has been regularly examined every week up to now, but trypanosomes have never been found therein.

EXPERIMENT NO. 305 (a). DONKEY. TOP OFF RIGHT EAR.

January 24, 1905. Injected subcutaneously 10 cubic centimetres of blood from dog, Experiment No. 333, containing trypanosomes in moderate numbers.

April 27. This animal remains in good health. Its blood has been examined every week, but trypanosomes have never been found in it.

EXPERIMENT NO. 371. GUINEA-PIG.

January 24, 1905. Injected subcutaneously 1 cubic centimetre of blood, mixed with citrate, from dog, No. 332, containing numerous actively motile trypanosomes.

March 28. Trypanosomes have not appeared in the animal's blood since inoculation. Re-inoculate animal by injecting a few drops of blood from guinea-pig, No. 372, containing the "Bugungu" trypanosomes in moderate numbers.

April 17. Trypanosomes have appeared in the blood to-day for the first time, 20 days after re-inoculation. The parasites are short, blunt pointed, and closely resemble the sleeping sickness trypanosome.

September 10. Up to to-day this animal has apparently been in good health; to-day it was found dead.

The following table shows the presence or absence of trypanosomes in the blood :—

Date.	Trypano- somes.	Date.	Trypano- somes.	Date.	Trypano- somes.
1905.		1905.		1905.	
Jan. 27 ...	—	April 17 ...	+	June 29 ...	+
Feb. 1 ...	—	" 27 ...	+	July 11 ...	+
" 17 ...	—	May 13 ...	+	" 23 ...	+
" 24 ...	—	" 27 ...	+	" 28 ...	+
March 18 ...	—	June 3 ...	+	Aug. 12 ...	+
" 28 ...	—	" 18 ...	+	" 24 ...	+
April 4 ...	—	" 24 ...	+	Sept. 4 ...	+

Post-mortem examination. Animal not emaciated. Eyes normal. Stomach and intestines full of food. All viscera appear normal. Spleen slightly enlarged. Trypanosomes could not be found in the blood. Lymphatic glands not enlarged.

EXPERIMENT No. 351. MONKEY (*Cercopithecus sp.*).

March 28, 1905. Animal's temperature has been taken every day for the last month, and has been found to be normal. Frequent blood-examinations have proved the absence of trypanosomes. Inoculate the monkey with "Bugungu" trypanosomes by injecting under the skin a few drops of blood from guinea-pig, No. 372.

April 6. Trypanosomes are present in the blood to-day for the first time. Animal's temperature is 105.4°.

May 14. Temperature irregular, varying between 99° and 103°. Trypanosomes have been constantly present in the blood since the first infection.

June 30. Animal has got progressively thinner and weaker. The eyes are normal, there are no enlarged superficial glands or œdema.

July 19. Animal died to-day.

The following table shows the result of the blood examinations in this case :—

Date.	Parasites in Blood.		Parasites in Cerebro-spinal fluid.		Date.	Parasites in Blood.		Parasites in Cerebro-spinal fluid.	
	Mal.	Tryp.	Strept.	Tryp.		Mal.	Tryp.	Strept.	Tryp.
1905.					1905.				
March 28 ...	+	—	May 21 ...	+	+
April 1 ...	+	—	" 30 ...	+	—
" 6 ...	+	+	June 8 ...	+	+
" 15 ...	+	+	" 18 ...	+	—
" 21 ...	+	+	" 26 ...	+	+
" 28 ...	+	+	July 7 ...	+	+
May 4 ...	+	+	" 14 ...	+	+
" 14 ...	+	+	" 19	+	...	—

Post-mortem made at death. Animal is thin. Pupils equal and normal. Superficial lymphatic glands not enlarged. On reflecting the dura mater, the surface of the cortex appears normal. Trypanosomes are not present in the cerebro-spinal fluid. Portions of brain are removed for minute examination. Heart appears normal. There is a little free fluid in the pericardial cavity. A drop of heart's blood contains trypanosomes in moderate numbers. The rest of the viscera appear normal. Spleen is enlarged to about twice the normal size.

The course of this Bugungu disease in a monkey very closely resembles that of sleeping sickness in the same animal. Trypanosomes were always present in the animal's blood, but never in large numbers.

EXPERIMENT No. 446. DOG (WHITE AND BROWN).

July 12, 1905. Injected subcutaneously a few drops of blood from monkey No. 351 containing the "Bugungu" trypanosome in scanty numbers.

August 4. Trypanosomes have appeared in the animal's blood to-day.

October 9. Animal remains in good health. Trypanosomes are constantly present in the blood. Many short stumpy forms of the parasite seen.

January 9th 1906. Animal does not seem quite so well as formerly. Appetite not good; he seems drowsy and listless and has lost flesh considerably. There is loss of power especially in the hind limbs. Eyes normal. Cervical lymphatic glands distinctly enlarged.

January 15. Animal remains in much the same state but is getting gradually weaker. He is always lying down and is apparently too weak to stand for long. Trypanosomes have always been seen in the blood ever since they first appeared, but never until lately in anything but scanty numbers. Glandular enlargement well-marked.

The following table shows the result of the blood-examinations :—

Date.	Parasites in Blood.			Date.	Parasites in Blood.		
	Pyro.	Mal.	Tryp.		Pyro.	Mal.	Tryp.
1905.				1905.			
July 12 ...	—	...	—	Dec. 6 ...	—	...	+
" 24 ...	—	...	—				
August 4 ...	—	...	+	1906.			
Sept. 6 ...	—	...	+	Jan. 9 ...	—	...	+
Oct. 9 ...	—	...	+	" 15 ...	—	...	+
Nov. 4 ...	—	...	+	" 20 ...	—	...	+

January 28. Animal moribund. Killed with chloroform.

Post-mortem examination at death. Heart and lungs normal. Spleen enlarged, soft and congested, weighs 4 ozs. Kidneys normal. Liver normal. All the glands of the body enlarged, both superficial, deep, abdominal and mesenteric. A blood-film taken after death did not show trypanosomes although a *Filaria* about the same size as *Filaria perstans*, but with a sharply pointed caudal extremity, was present. This *Filaria* seems similar to that found formerly in the blood of monkeys and described in the last Report. No traces of an adult *Filaria* could be found. Brain appeared normal to the naked eye. Cerebro-spinal fluid not increased. Trypanosomes were numerous in the deposit left after centrifuging some blood stained cerebro-spinal fluid. Emulsions of portions of the brain in normal citrate-solution showed trypanosomes to be present in scanty numbers. Sections of the brain, stained by Leishman's method, showed well-marked small-celled infiltration around the blood vessels. This change was more marked in the deeper parts of the brain-substance than in the cortex. (See plate I.)

EXPERIMENT NO. 461. CAT (TAME, BLACK AND WHITE).

July 19, 1905. Injected subcutaneously a few drops of blood from monkey No. 351 containing trypanosomes in scanty numbers.

August 14. Trypanosomes have appeared in the blood to-day for the first time.

January 22, 1906. Animal remains in good health, trypanosomes have been present in the blood almost continually since their first appearance.

The following table shows the results of the blood examinations :—

Date.	Parasites in Blood.	Date.	Parasites in Blood.	Date.	Parasites in Blood.
	Trypano-somes.		Trypano-somes.		Trypano-somes.
1905.		1905.		1905.	
July 19 ...	—	Aug. 19 ...	+	Nov. 25 ...	+
" 27 ...	—	" 31 ...	+	Dec. 10 ...	+
" 30 ...	—	Sept. 11 ...	+	" 27 ...	+
Aug. 2 ...	—	" 20 ...	—		
" 4 ...	—	" 27 ...	+	1906.	
" 6 ...	—	Oct. 7 ...	+	Jan. 8 ...	+
" 10 ...	—	" 20 ...	—	" 22 ...	+
" 14 ...	+	Nov. 1 ...	—		

SECTION OF BASAL GANGLIA OF BRAIN OF DOG N° 446,
 SHOWING MARKED SMALL-CELLED INFILTRATION AROUND
 THE BLOOD VESSELS. THIS DOG WAS INOCULATED
 WITH THE "BUGUNGU" STRAIN TO TRYPANOSOME
 AND DIED SEVEN MONTHS AFTER INFECTION.

*Drawn with camera lucida from a section stained by Leishman's method
 (Zeiss 16 mm Apochromatic obj. N° 8 comp. ocular).*



EXPERIMENT NO. 454. RAT (BLACK AND WHITE).

July 17, 1905. Injected a few drops of blood, mixed with normal citrate-solution, from guinea-pig No. 371 (Bugungu) into this rat.

July 27. Trypanosomes first appeared in this animal's blood to-day. They are very scanty in number.

October 24. There is some weakness of the animal's hind limbs to-day. Trypanosomes have not been found in the blood since August 4.

November 1. There is very marked paralysis of both hind limbs. Except for this the animal seems fairly well.

November 15. Animal died this morning. The paralysis never spread beyond the hind limbs. During the last few days the animal's coat became very dirty and lousy.

The following table shows the result of the blood examinations :—

Date.	Trypano- somes.	Date.	Trypano- somes.	Date.	Trypano- somes.
1905.		1905.		1905.	
July 20 ...	—	Aug. 6 ...	—	Sept. 20 ...	—
" 21 ...	—	" 8 ...	—	" 27 ...	—
" 23 ...	—	" 14 ...	—	Oct. 4 ...	—
" 24 ...	—	" 19 ...	—	" 17 ...	—
" 25 ...	—	" 21 ...	—	" 19 ...	—
" 27 ...	+	" 23 ...	—	" 24 ...	—
" 29 ...	+	" 27 ...	—	Nov. 1 ...	—
" 31 ...	+	Sept. 1 ...	—	" 12 ...	—
Aug. 2 ...	+	" 6 ...	—	" 15 ...	—
" 4 ...	+	" 13 ...	—		

Post-mortem. Examination made about three hours after death. Animal is emaciated; covered with lice. Eyes appear normal. No marked enlargement of the superficial lymphatic glands. The brain and spinal cord appear normal to the naked eye. An emulsion of brain-matter in normal citrate-solution shows numerous trypanosomes even without centrifuging. Stained films of this emulsion show vacuolated trypanosomes in large numbers. Similar emulsions of the spinal cord show trypanosomes in scanty numbers. The superficial lymphatic glands are slightly enlarged. The spleen and other viscera appear quite normal. Trypanosomes are not present in a blood-film, but have been found in very scanty numbers after centrifuging the heart's blood. Sections of brain stained by Leishman's method show numerous trypanosomes all through the brain-substance. Trypanosomes have not been seen in the blood-vessels of the brain. A small-celled infiltration is evident around these blood-vessels, more marked in the deeper parts than in the brain-cortex.

The course of the disease, the subsequent paralysis, the *post-mortem* appearances and the aspect of the sections of the brain in this animal are in every way similar to what we have found in rats infected with the trypanosome of sleeping sickness. Apart from other evidence, this experiment shows that the Bugungu trypanosome is identical with the trypanosome of sleeping sickness.

VIII.—*The Trypanosome of the Jinja cattle disease. Further inoculation experiments on White Rats, Guinea-pigs, &c. Effect of Drugs on animals inoculated with this parasite.*

In Report No. VI., p. 11, a good deal of information was given concerning a disease which had proved very fatal to a large herd of cattle in Usoga. This disease was found to be due to the presence of a trypanosome in the blood of these cattle,

and from experimental inoculations with this trypanosome on a number of different animals it seemed likely that this trypanosome was either identical with *Trypanosoma Brucei* or else a very closely allied species.

In the following tables we give the results of some further inoculation experiments which we have conducted on white rats and guinea-pigs.

WHITE RATS.—Incubation period : shortest, 4 days ; longest, 8 days ; average, 5 days. Total length of the disease from day of inoculation to day of death : shortest, 10 days ; longest, 29 days ; average, 20 days.

Course of the disease.—Trypanosomes appear scantily in the blood about the fifth day, and from this time forward, as a rule, the parasites become more and more numerous until at death they outnumber the red blood corpuscles. Sometimes we have noticed that early in the disease at about the 10th to the 15th day the parasites temporarily disappear from the blood-stream, but that in such cases the trypanosomes always reappear again, and that then the disease runs its normal course. Three of these rats showed exhibited well-marked corneal opacity which appears within a few days of death. Two of them showed paralysis of the hind limbs within a day or two of death. As a rule, the rats seemed in good health up to 48 hours of death. Death occurred somewhat suddenly and was accompanied by convulsive movements, and the appearance of blood-stained froth around the mouth.

The *post-mortem* appearances were very constant. Hæmorrhages into the substance of both the lungs were present in every case, sometimes extensively. There was no enlargement of the lymphatic glands. The spleen was considerably enlarged in every case. The heart appeared quite normal. In many cases the bladder contained blood-stained urine, and in these cases the kidneys were hæmorrhagic.

GUINEA-PIGS.—Incubation period : shortest, 6 days ; longest, 19 days ; average, 9 days. Total length of the disease : longest, 93 days ; shortest, 9 days ; average, 35 days.

Course of the disease.—Trypanosomes having once appeared in the animal's blood could in every case be found there till death. Parasites were always numerous in the blood and at death were invariably present in large numbers. Two of these animals showed paralysis of the hind quarters shortly before death. Opacity of the cornea was not observed in any instance. As in the case of white rats, death often seemed to occur very suddenly.

The *post-mortem* appearances consisted of hæmorrhages into the lungs in several cases. Petechiæ over the surface of the

heart were often noticed; in one case there was marked pericardial effusion. The spleen was always enlarged and generally to a considerable extent. The superficial lymphatic glands were sometimes slightly enlarged.

TABLE X.

White Rats inoculated with the Trypanosome of the Jinja cattle disease.

No. of Experiment.	Date of Inoculation.	Date of appearance in Peripheral Blood.	Result.
444	July 2 ...	July 6 ...	Died July 29. (27 days.) Largo spleen. Trypanosomes swarming in the blood. Lungs full of hæmorrhages. Urine blood stained.
467	Aug. 10 ...	Aug. 16 ...	Died Sept. 8. (29 days.) Autopsy as above.
469	" 25 ...	" 31 ...	Died Sept. 11. (17 days.) Autopsy as above, but liver also enlarged. Lymphatic glands somewhat enlarged.
475	Sept. 8 ...	Sept. 12 ...	Died Sept. 24. (16 days.) Autopsy as above.
476	" 11 ...	" 19 ...	Died Sept. 28. (17 days.) Autopsy as above.
483	" 20	Died Oct. 15. (25 days.) Autopsy as above, with opacity of both corneæ.
484	" 20	Died Oct. 15. (25 days.) Autopsy as above. Urine normal.
485	" 20	Died Oct. 7. (17 days.) Autopsy as above. Eyes normal.
486	" 25 ...	Sept. 29 ...	Died Oct. 10. (15 days.) Animal showed paralysis of the hind limbs for a day or two before death. Autopsy as before.
487	" 28 ...	Oct. 5 ...	Died Oct. 19. (21 days.) Showed paralysis of hinder extremities before death. Trypanosomes swarmed in the blood at death. Spleen very large. Glands slightly enlarged. Lungs show numerous hæmorrhages. Eyes normal. Urine not blood-stained.
495	Oct. 4 ...	" 9 ...	Died Oct. 29. (25 days.) Autopsy as above. Opacity of right cornea. No paralysis before death.
501	" 7 ...	" 12 ...	Died Oct. 30. (23 days.) Autopsy. Eyes normal, otherwise as above. No paralysis.
515	" 29	Died Nov. 8. (10 days.) Autopsy as above. Liver also larger than normal. Urine blood stained. Eyes normal. No paralysis.

TABLE XI.

Guinea-pigs inoculated with the Trypanosome of the Jinja cattle disease.

No. of Experiment.	Date of Inoculation.	Date of appearance in Peripheral Blood.	Result.
329	Nov. 22...	Nov. 29 ... (7 days.)	Died on Dec. 24. Swarming with parasites. Hæmorrhages into lungs. Spleen slightly enlarged.
338	Dec. 4...	Dec. 14 ... (10 days.)	Died Jan. 7, as above.
337	" 4...	Dec. 14 ... (10 days.)	" " 25 "
366	Jan. 12...	Jan. 20 ... (8 days.)	" " 27 "
367	" 12...	Jan. 20 ... (8 days.)	" Feb. 9 "
388	March 28...	April 4 ... (7 days.)	" May 7 "
400	April 15...	April 27 ... (12 days.)	Died July 29. Paralysis of hind limbs. Trypanosomes swarming in the blood. Spleen much enlarged.
401	" 15...	May 3 ... (18 days.)	Died May 28. Paresis of hind quarters. Spleen only slightly enlarged. Lungs hæmorrhagic.
402	May 7...	May 13 ... (6 days.)	Died June 12. Swarming with trypanosomes. Spleen slightly enlarged. Lungs hæmorrhagic.
426	June 18...	July 1 ... (13 days.)	Died July 19. Spleen enlarged. Trypanosomes very numerous.
427	" 18...	June 24 ... (6 days.)	Died July 6. Spleen slightly enlarged. Trypanosomes very numerous.
435	" 24...	July 1 ... (7 days.)	Died July 3. Spleen not enlarged. Trypanosomes very numerous.
465	July 29...	Aug. 6 ... (8 days.)	Died August 25. Spleen slightly enlarged. Trypanosomes very numerous.
488	Sept 28...	Oct. 9 ... (11 days.)	Died November 5. Spleen enlarged.

MONKEYS.—Incubation period: shortest, 4 days; longest, 10 days; average, 6 days.

Total length of the disease from day of inoculation to day of death: shortest, 28 days; longest, 86 days; average, 56 days.

Course of the disease.—The appearance of the trypanosomes in the blood about the sixth day is marked by a sharp rise of temperature. Trypanosomes are always to be found in the blood from this time onwards, and are often numerous. For the first month or so the temperature chart shows sharp elevations every few days. About a month before death marked daily variations of temperature begin to occur, and become more and

more marked. Trypanosomes are numerous in the blood at death. We have never observed any symptoms of paralysis or eye changes in such monkeys.

On *post-mortem* examination the lungs often show small hæmorrhages, petechial hæmorrhages are found on the heart, the abdominal lymphatic glands are generally enlarged, the liver was often found to be fatty, and the spleen was always considerably larger than normal.

The following table shows the results of inoculating six monkeys with this trypanosome :—

TABLE XII.

Monkeys Inoculated with the "Jinja" Cattle Trypanosomes.

No. of Animal.	Date of Inoculation.	Date of appearance in Blood.	Result.
317	Sept. 4 ...	Sept. 11 ...	Died Nov. 22. Trypanosomes always numerous in blood. Spleen and abdominal glands enlarged. Petechial hæmorrhages in lungs, heart, and stomach.
322	Oct. 26 ...	Nov. 1 ...	Died Nov. 23. Trypanosomes always numerous. Spleen somewhat enlarged. Other viscera very anæmic.
344	Dec. 11 ...	Dec. 16 ...	Died Jan. 12. Trypanosomes always numerous. Spleen enlarged. Liver shows points of pus all through its substance. Small abscess size of cherry between liver and right kidney. Mesenteric glands enlarged.
384	Feb. 22 ...	March 4 ...	Died May 19. Trypanosomes always very numerous. Organs anæmic. Petechiæ on heart. Spleen markedly enlarged.
335	Dec. 4 ...	Dec. 16 ...	Died Jan. 25. Trypanosomes always present in the blood.
330	Nov. 23 ...	Nov. 27 ...	A large dose of arsenic caused trypanosomes to disappear, and cured the animal.

The effect of Drugs upon Monkeys suffering from the "Jinja" Cattle Trypanosome.

We have already shown that the "Jinja" cattle trypanosome is always fatal to monkeys, and that during the course of the disease in these animals the trypanosomes are constantly present in the animal's blood in considerable numbers. We have tried arsenic and trypanoth on a few monkeys infected with this trypanosome with the view of ascertaining whether these drugs can in any way modify the course of the disease.

Arsenic.—(1.) As a curative agent. We have tried this drug on two monkeys infected with this trypanosome. In the first case a maximum dose of arsenic was injected into the animal four days after the trypanosomes had first appeared in the blood, with the result that the animal was cured and was well $4\frac{1}{2}$ months after the arsenic had been given, trypanosomes never having reappeared in the blood. A second infected monkey was given a similar dose of arsenic after trypanosomes had been present in the animal's blood for 12 days, but in this case the parasites reappeared in the blood, and the animal died $2\frac{1}{2}$ months after infection.

(2.) As a prophylactic. We found arsenic quite useless in this respect. A maximum dose of it given 24 hours before inoculating the animal with this trypanosome only doubled the length of the incubation period of the disease.

Trypanroth.—A maximum dose of this drug injected into a monkey infected with this trypanosome had the effect of causing the parasites to disappear for four days only. The disease ran its usual fatal course.

A monkey was inoculated with this trypanosome 48 hours after it had been given a maximum dose of trypanroth. This previous dose of trypanroth had no power to protect the animal against the disease; trypanosomes appeared in the blood at the usual time, and the disease terminated fatally as usual.

EXPERIMENT No. 330. MONKEY (*Cercopithecus* sp.). WEIGHT,
4.98 KILOGRAMMES.

November 23. Inject one cubic centimetre of blood containing trypanosomes from the heart of monkey 317, obtained *post-mortem*. (Monkey 317 died in three months from the "Jinja" cattle disease.)

November 27. Trypanosomes present in the blood to-day. Temperature 107° .

November 30. Trypanosomes present in the blood in very large numbers. Temperature 106° . Inject arsenic 12 milligrammes, equivalent to 1 milligramme per 400 grammes monkey. Animal's blood examined $2\frac{1}{2}$ hours after the injection. No living trypanosomes can be found in the blood. A blood-film shows a very few parasites. 4.30 p.m. (seven hours after the arsenic); temperature 101° . Blood examined; trypanosomes absent. Animal sits in a doubled-up posture, refuses food.

December 1. Animal still seems sick. Diarrhoea present. Marked thirst, refuses food. Trypanosomes absent from a blood-film.

December 5. Animal seems to have recovered from the arsenic. Trypanosomes absent from blood.

March 1. Animal's blood has been examined regularly once a week for the last three months. Trypanosomes have never been found. Animal is thin, but otherwise is in good health. The temperature has remained generally about normal.

April 6. Trypanosomes have now been absent from the blood for more than four months. Animal is getting very thin and beginning to show a swinging temperature. Reinject 1 cubic centimetre of blood taken from monkey 384 containing the "Jinja" trypanosome in large numbers.

April 14. Trypanosomes have again appeared in the blood to-day, eight days after the second inoculation.

April 16. Animal very sick, lies on its side, eats very little.

The following table shows the presence or absence of trypanosomes in the blood :—

Date.	Parasites in Blood.		As ₂ O ₃ . 12 Milli-grammes.	Date.	Parasites in Blood.		As ₂ O ₃ . 12 Milli-grammes.
	Mal.	Tryp.			Mal.	Tryp.	
Nov. 25 ...	+	—	...	Jan. 6 ...	+	—	...
" 27 ...	+	+	...	" 17 ...	+	—	...
" 30 ...	+	+	12	" 24 ...	+	—	...
(10 a.m.)				" 30 ...	+	—	...
Nov. 30 ...	+	—	...	Feb. 8 ...	+	—	...
(12 noon.)				" 14 ...	+	—	...
Dec. 1 ..	+	—	...	" 21 ...	+	—	...
" 7 ...	+	—	...	March 1 ...	+	—	...
" 11 ...	+	—	...	" 8 ...	+	—	...
" 18 ...	+	—	...	" 17	—	...
" 23 ...	+	—	...	" 28	—	...
" 30 ..	+	—	...	April 6	— (reinoculated).	...
				" 14	+	...

EXPERIMENT NO. 361. MONKEY (*Cercopithecus sp.*).

To note the effect of a single large dose of arsenic on a monkey infected with the trypanosome of the "Jinja" cattle disease.

March 18. Weight of monkey 2·381 kilogrammes. Blood examined and found to contain malaria but no other parasite.

March 28. Animal's temperature has been taken night and morning for the last ten days and has been found to be normal. Inoculate monkey with the "Jinja" trypanosome, by injecting a few drops of blood from monkey 384, in which the parasites are active and numerous.

April 3. Temperature has suddenly run up to 108°. Trypanosomes are numerous in the blood to-day, six days after inoculation.

April 15. Trypanosomes have now been constantly present in the blood for ten days. Give arsenic 6 milligrammes, equivalent to 1 milligramme arsenic per 400 grammes monkey. Trypanosomes disappeared from the blood in 2½ hours.

April 16. Animal not much the worse for the arsenic.

May 3. Trypanosomes have again appeared in the blood to-day (19 days after arsenic).

May 25. Animal died in the night, during a heavy storm. The monkey had been getting steadily thinner and showed a swinging temperature for the last fortnight.

The following table shows the result of the blood examinations :—

Date.	Parasites in Blood.			—
	Fil.	Mal.	Tryp.	
March 28	...	+	—	...
April 3	...	+	+	...
" 10	...	+	+	...
" 15 (10.45 a.m.)	...	+	+	...
" " (11.45 ")	...	+	+	As ₂ O ₃ , 6 milligrammes.
" " (12.45 p.m.)	...	+	+	...
" " (1.15 ")	...	+	—	Trypanosomes very scanty.
" 19	...	+	—	...
" 21	...	+	—	...
" 28	...	+	—	...
May 3	...	+	+	...
" 5	...	+	+	...
" 14	...	+	+	...
" 25	+	Autopsy.

Autopsy made about eight hours after death. Trypanosomes numerous and active in the heart's blood. Animal thin. No glandular enlargement. Eyes normal. Spleen enlarged to about three times the normal size. Smears of spleen show numerous trypanosomes. Other organs apparently healthy.

It is interesting to compare this experiment with experiment 330. The two animals were given exactly similar doses of arsenic, viz., 1 milligramme of arsenic per 400 grammes weight of monkey. In experiment 330 the drug was given four days after the first appearance of the trypanosome in the blood, with the result that the animal was cured. In the present experiment the arsenic was given 12 days after the first appearance of the parasite, with the result that the trypanosomes only disappeared for a time, reappearing again 19 days after the drug had been administered.

EXPERIMENT NO. 335. MONKEY (*Cercopithecus sp.*). WEIGHT, 1.247 KILOGRAMMES.

To note the effect of arsenic as a prophylactic in the case of the "Jinja" trypanosomes.

December 3 (2 p.m.). Examine blood. Trypanosomes are absent. Malaria present. Give arsenic 5 milligrammes (equivalent to 1 milligramme arsenic per 250 grammes monkey).

December 4 (10 a.m.). Animal seems sick, has been much purged in the night. Inoculate it with "Jinja" trypanosome, by injecting a few drops of blood from guinea-pig 329, in which the parasites are very numerous.

December 16. Temperature 107°. Trypanosomes are present in the blood to-day for the first time (12 days after inoculation). Up to to-day, animal's blood had been examined every other day, but always with a negative result.

Date.	Parasites in Blood.		As ₂ O ₃ in milligrammes.
	Mal.	Tryp.	
Dec. 3	—	5
" 4	Inoculate with trypanosomes ("Jinja").		
" 11	—	...
" 16	+	...
" 19	+	...

EXPERIMENT No. 339. MONKEY (*Cercopithecus sp.*). WEIGHT,
1.460 KILOGRAMMES.

CONTROL ON EXPERIMENT 335.

December 4. Examine blood. Trypanosomes are absent. Malaria present. Inoculate monkey with "Jinja" trypanosome, by injecting a few drops of blood from guinea-pig 329, in which the parasites are very numerous.

December 7. Blood examined. Trypanosome absent. Malaria present.

December 8. Temperature 106.4°. Trypanosomes are present in the blood to-day for the first time (four days after inoculation).

Remarks.—The above experiments show that even a maximum dose of arsenic given to a monkey twenty hours before he is inoculated with the trypanosome of the "Jinja" cattle disease, is powerless to protect the animal against infection, although it has the effect of considerably lengthening the incubation period of the disease.

EXPERIMENT No. 317. MONKEY (*Cercopithecus sp.*). WEIGHT,
1.5 KILOGRAMMES.

To note the effect of subcutaneous injection of a solution of trypanroth in a monkey suffering from the parasite of the "Jinja" cattle disease.

September 4. Examine blood-film. Trypanosomes are absent. Inoculate monkey with 1.5 cubic centimetre blood from monkey No. 315, containing numerous trypanosomes.

September 11. Trypanosomes are present in the blood to-day for the first time (seven days after inoculation). Temperature, 105.6°.

October 26. Trypanosomes have been constantly present in the animal's blood for the last six weeks. Injected 10 cubic centimetres of 1 per cent. solution of trypanroth at 12.30 p.m.

November 1. Trypanosomes have reappeared in the animal's blood to-day.

November 19. Animal died to-day. Trypanosomes have been present in the blood in increasing numbers since November 1.

The following table shows the result of the blood examinations and the result of this injection on the trypanosomes :—

Date.				Parasites in Blood.		No. of Trypanosomes per c. milli- gram.	Leucocytes per c. milli- gram.
				Mal.	Tryp.		
Sept.	9	—	—
"	11	—	+
"	15	—	+
"	21	—	+
"	22	—	+
"	20	—	+
Oct.	7	—	+
"	14	—	+
"	21	—	+
"	26	—	+	11,250	15,000
"	27	+	400	40,600
"	28	—	...	31,200
"	29	—	...	29,600
"	31	—	...	18,700
Nov.	1	+	30	12,000
"	2	+	280	9,800
"	4	+	1,020	17,000
"	7	+	7,000	13,000
"	14	+
"	19	+

EXPERIMENT No. 320. MONKEY (*Cercopithecus sp.*). WEIGHT,
2·51 KILOGRAMMES.

To note the effect of trypanroth (Ehrlich) on a monkey, and further to note whether this drug has any prophylactic effect against infection with the "Jinja" cattle disease.

October 26. Inject subcutaneously 20 cubic centimetres of a 1 per cent. solution of trypanroth.

October 27. Animal shows some subcutaneous pigmentation. General health is good.

October 28. Subcutaneous pigmentation very marked indeed.

December 2. There is still a trace of pigmentation to be seen. The drug does not seem to have affected the animal's health in any way. Some thickening can be felt at the seat of inoculation. Inject subcutaneously a further dose of 25 cubic centimetres of 1 per cent. trypanroth.

December 4. There is very intense pigmentation present. Inoculate the animal with the "Jinja" trypanosome by injecting a few drops of blood from guinea pig 329, which contains trypanosomes in large numbers.

December 14. Trypanosomes are present in the animal's blood to-day. Animal's temperature has risen suddenly to 105·6°.

Remarks.—These two experiments show that a large single dose of trypanroth simply causes a very temporary disappearance of the parasites from the blood in the case of an animal infected with the trypanosome of the "Jinja" cattle disease, and that a similar large dose of trypanroth given 48 hours before inoculating an animal with this disease has no prophylactic effect.

17. REPORT ON EXPERIMENTS TO ASCERTAIN
THE ABILITY OF TSETSE FLIES TO
CONVEY *TRYPANOSOMA GAMBIENSE* from
Infected to Clean Monkeys, and on an Intra-Corpus-
cular Stage of the Trypanosoma.

BY PHILIP H. ROSS, M.R.C.S., L.R.C.P. LOND., D.P.H.
(Camb.).

Between the months of July and December, 1904, two experiments were carried out, to see whether the tsetse flies found near Kibwezi are able to convey the *Trypanosoma gambiense* from an infected to a clean monkey. The first of these experiments was made with *Glossina fusca*, the interval between feeding on infected and clean monkey being eight hours. The second experiment was with *Glossina pallidipes*, the interval in this case being 24 hours.

At first, before the experiments could be begun, continual delays arose from various causes, of which the most important

and the one which led to the longest delay was the fact that all the monkeys sent me for experimental purposes were in various stages of Piroplasmosis. This has already been the subject of a note in the *Journal of Hygiene* (vol. V., No. 1, January, 1905). In all cases the monkeys were kept in fly-proof cages onwards from their arrival. When at last the temperature of the monkeys had become nearly normal experiments were started and were carried out in the following manner :—

The flies were caught at Kibwezi by boys, who put them in boxes and sent them by rail, at first to Makindu, latterly to Nairobi. On arrival, each fly was caught separately in a specimen glass and examined to decide to which species it belonged. Almost always only *Glossina fusca* and *Glossina pallidipes* were found; very rarely *Glossina longipennis* was caught. Each species was put in a separate box and fed at once on a monkey (called hereafter the "fresh-fly monkey"). A separate fresh-fly monkey was used for each species of fly.

I had originally intended to carry out the experiments as they had been done at the laboratory at Entebbe, with the addition of controls; but at Lieut.-Colonel Will's suggestion, the flies, after their first feed on the fresh-fly monkey, were starved for four days. It was found that if the period of starvation were prolonged beyond four days, very few flies survived. At the end of four days the flies were divided into two lots, one of which was used for the experiment, the other for a control. The flies for the experiment were now fed on the infected monkey, and after the proper interval, fed again on the clean monkey. The control consisted in taking the other box of flies and feeding them twice on the control monkey at the same intervals. These flies, therefore, were fed at the same time and as often as the flies in the actual experiment, and so, as long as the control monkey remained uninfected, gave some guarantee that the initial starvation had been sufficient to prevent them from conveying any *Trypanosoma* with which they might have been infected before capture. The experimental and control monkeys were of course the same throughout the experiment, though at first several experiments were abortive through the death of one or other of the monkeys. The infected monkey had to be replaced several times in the *Glossina fusca* experiment, but in the case of *Glossina pallidipes*, one monkey lasted till the experiment came to an end through lack of flies.

The infected monkeys came from Entebbe at the beginning of May. They had all been injected with cerebro-spinal fluid from cases of sleeping sickness, such fluid showing many active *Trypanosomata*. Of the four monkeys sent, one proved to be uninfected, but was infected at Makindu from one of the other monkeys. The strain was kept up by injecting fresh monkeys with a drop or two of blood from the finger of one or other of these three monkeys.

EXPERIMENT NO. 1.

To see whether the *Glossina fusca* can convey the *Trypanosoma gambiense* from an infected to a clean monkey when fed on the clean monkey eight hours after feeding in the infected monkey.

In this experiment Monkey No. 9 was used throughout as fresh-fly monkey. Between July 1 and November 20, 348 flies were fed on this monkey, but it never became infected and is still healthy. Five infected monkeys were used, Nos. 2, 12, 4, 28, and 27.

Between July 18 and November 28, Monkey No. 13 had 368 flies fed on it, eight hours after feeding on the infected monkey. It never showed Trypanosomata in its blood until its death on November 28, nor were any signs of trypanosomiasis found on *post-mortem*. It apparently died of piroplasmiasis, as did many other monkeys coming from the same place.

Monkey No. 11 was used as control, and had 761 flies fed on it between July 5 and December 5. It has never shown Trypanosomata in its blood nor any sign of trypanosomiasis. This experiment was ended by death of clean monkey.

EXPERIMENT NO. 2.

To see whether the *Glossina pallidipes* can convey the *Trypanosoma gambiense* from an infected to a clean monkey when fed on the clean monkey 24 hours after feeding on the infected monkey.

Fresh-fly Monkey No. 22 had 85 flies fed on it between September 11 and November 10. Trypanosomata were found in the blood on November 20, seven days after feeding had been begun. The monkey died on November 29, and shewed no macroscopic lesion on a *post-mortem* examination.

Infected Monkey No. 24 had 296 flies fed on it between September 15 and December 10.

Between September 15 and December 5, clean Monkey No. 29 had 205 flies fed on it 24 hours after feeding on the infected monkey. It has never shewn Trypanosomata in its blood nor any sign of trypanosomiasis, and is still healthy.

Control Monkey No. 28 had 257 flies fed on it between September 14 and November 17. It has never shewn Trypanosomata in its blood nor any sign of trypanosomiasis, and is still healthy.

This experiment was ended by the infection and death of the fresh-fly monkey; no other being available to replace it. Throughout the experiments a routine weekly examination of the blood was made.

There is not sufficient material in these experiments to come to any definite conclusions. The results in the *Glossina fusca*

experiment were entirely negative, and I am inclined to think that probably this fly does not convey any species of Trypanosoma. Whereas in the second experiment 85 flies fed over 60 days resulted in Trypanosomata being found in the blood on the seventieth day, in this case 348 flies feeding over five months and three weeks did not result in infection, although these flies came from the same noted fly belt as the *Glossina pallidipes*.

From the second experiment it is evident that the *Glossina pallidipes* can convey a Trypanosoma when fed on a monkey at least 16 to 18 hours after it could possibly have fed last. It is true that it did not succeed in conveying the *Trypanosoma gambiense* under the conditions of the experiment, but that by no means proves that it could not do so in Nature.

Round the shores of Lake Victoria, the *Glossina palpalis* is abundant and it is presumably this fly that there conveys the Trypanosomata of cattle, donkeys, &c. (e.g. the "Jinja" Trypanosoma of the Royal Society's Reports). But this fly also conveys the *Trypanosoma gambiense*. At Kibwezi there is the *Glossina pallidipes* which has shown itself capable of conveying a Trypanosoma, and from the analogy of the *Glossina palpalis* in Uganda, it seems probable that the Kibwezi fly (*Glossina pallidipes*) will also be shown to be able to convey the *Trypanosoma gambiense*.

The results of the fresh-fly experiments make me inclined to think that there must be something more than direct transference with a soiled proboscis and that the mere number of flies feeding cannot be of the first importance. But there are also objections to the theory of a developmental phase in the fly corresponding to that of malaria in the mosquito. For I have had flies which, surviving in their boxes for weeks, were fed regularly during that time on blood rich in Trypanosomata, and yet they have never conveyed the parasite. It is as difficult to see why, given a developmental phase, these flies did not convey the disease, as it is to see why they failed, if it be only a case of direct transference. There is another possibility and that is that there may be an hereditary transmission from parent fly to offspring. I have never been able to get larvæ from either *Glossina fusca* or *Glossina pallidipes*, so have not been able to work at the question; but in the light of Schaudinn's work it would seem to be worth trying, and if I can get the larvæ I hope to be able to carry out some experiments.

Having in view Schaudinn's work, I gave up using a low power when searching microscopically for Trypanosomata and used the oil-immersion entirely. But I have never seen any sign of an intracorpuseular stage of the Trypanosoma. On several occasions I have examined the blood of infected monkeys at intervals during the night, but have found the same results as when examined by day. There does not appear to be any increase in number nor could I find intracorpuseular forms.

I had at one time some monkeys whose blood showed a marked infection with *Plasmodium Kochi*. In a fresh specimen, flagellation occurred almost before one could get the lens focussed. I also examined the blood of these monkeys at intervals during the night, in the hopes of finding a *Trypanosoma* form. But the results were as negative as were those of the *Trypanosoma gambiense* in the opposite direction.

Through the kindness of Mr. Orloff (Assistant Surgeon at Makindu) Colonel Bailey and Mr. Percival (Game Ranger), I have been able to examine blood-slides from a fair number of animals. Most of the slides have of course been quite negative, but there are some results which are worth recording.

- (1.) Blood of Mpala, shot and slide taken by Mr. Orloff. In this slide I found intracorpuseular bodies resembling in shape a mature *Proteosoma*, but showing no pigment. They stained blue with Leishman's, and showed small chromatin dots scattered throughout. The bodies were fairly numerous and a few were found free, presumably from damage to the blood-cells in spreading the film. Besides these bodies, there were a very few *Spirillum*-like bodies. These were about 18μ long, sharply pointed at both ends, but considerably thicker (1μ) than the human *Spirilla*. Whether there was any connection between the two parasites in this animal I am unable to say, but the results in the two cases following seem to render it unlikely.
- (2.) Blood of Coke's Hartebeest; shot and slide taken by Mr. Percival. In this I found the *Spirillum*-like bodies as described above, considerably more numerous than in the former case, but still scanty. Prolonged search failed to show any intracorpuseular bodies.
- (3.) Blood of Thomson's Gazelle, shot and slide taken by Colonel Bailey. Here again I found the *Spirillum* as above, but could detect no intracorpuseular bodies.
- (4.) Blood of Zebra. Slides taken by Mr. Stordy, Chief Veterinary Officer. The zebras were dying on Colonel Bailey's zebra farm at Athi river, from *Strongylus armatus*. In one of the slides brought to me by Mr. Stordy I found *Piroplasmata* similar in appearance to the parasite of African Coast Fever. This may prove of importance if it can be shown that the game is the source of infection of the various *Piroplasmoses* of which this country is full. But the difficulties in the way of experiments in this direction are very great.

The Flies. Both *Glossina fusca* and *Glossina pallidipes* were caught near Kibwezi Station. The country there is hilly, much of it covered with dense bush. The Kibwezi river rises in

springs near the station and runs down the bottom of the valley. The *Glossina pallidipes* was caught on the edge of the bush or in open spaces where animals, chiefly goats, were grazing, but never at any great distance from the water. There seems to be a marked seasonal prevalence in this fly; until towards the end of August hardly a specimen of it was caught, but from August to November more flies of this variety than of *Glossina fusca* were caught. This period is the driest season of the year. This fly (*Glossina pallidipes*) has a very wide distribution in this country and seems to extend along a great part of the Athi and Kiboko rivers. Major Pope Hennessy has sent me specimens from the Gosha forest in Jubaland.

In contrast to the habits of the *Glossina pallidipes* are those of the *Glossina fusca*. This fly can be most easily found on the slightly damp black cotton soil between the boulders on the hill-side. The *Glossina pallidipes* attacks as soon as one gets among them, but the *Glossina fusca* shows no inclination to bite men. Christy (Reports of Expedition to the Congo, 1903-1904) suggests that the *Glossina fusca* bites at night, but I have no information on the subject. It can only be said that this fly shows little inclination to bite by day, is usually found on damp soil, and its numbers do not seem to be affected by the presence or absence of stock. It has been caught throughout the year but is most numerous in the wet season.

The *Glossina longipennis* has not been found at Kibwezi, but at a station further down the line (Kinani) has been caught in quantities. Along the railway line and the old caravan road, where there is little or no bush, the fly apparently rests on the red soil, flying up and attacking any animal or man passing by. It is as troublesome as the *Glossina pallidipes* in this way, but apparently does not bite all day; for one can go along the line at midday without seeing a fly, but after 4 p.m. one is immediately attacked. This fly enters the train regularly at night and can be found flying about the lamp. My Indian Assistant, Compounder Pillay, through whom I have obtained most of my information about the flies, tells me that he has never found a *Glossina longipennis* come on board the train in the daytime, but at night they are attracted by any light and will then bite. This fly is found between the Tsavo and the Mtoto Ndi rivers. A few specimens have been caught outside these limits, but they have been in the railway stations and have evidently been carried by the train. I have not been able to find out anything about the seasonal prevalence of this fly.

18. REPORT ON SLEEPING SICKNESS IN UNYORO AND THE NILE VALLEY.

BY A. D. P. HODGES, M.D. LOND., MEDICAL OFFICER,
UGANDA PROTECTORATE.

I.—*Summary of Report.*

The route traversed after leaving Hoima was :—Masindi, Fajao, Foweire, Fajao, Wadelai, Lake Albert (by water), Wadelai (by water), Nimule (by water), Gondokoro.

On my arrival at Hoima I saw cases of undoubted sleeping sickness which had been brought in from Bugungu (Bachopi) by Dr. Pooley, and had been subsequently seen by Capt. Greig, I.M.S., of the Sleeping Sickness Commission. These cases were in all stages of the disease, which had been contracted locally.

The presence of sleeping sickness in epidemic form in N.W. Unyoro was therefore certain, and, as I found that Dr. Pooley had just recently passed through the Butiaba, Fajao lines of country, and Capt. Greig was then again traversing a part of it, I was induced, with the permission of the Principal Medical Officer, to alter my intended route along that line to one further inland, including Masindi, Fajao and Foweire, in order to ascertain, if possible, the extent of the epidemic, the prevailing local conditions likely to influence its spread, and its origin; especially, whether it had travelled directly by the supposed fly-belt along the Nile from the Victoria Nyanza epidemic. I was further persuaded to take this line by hearing that there were, or had been, a good many sick people at places near the Masindi-Fajao road.

The centre of the present epidemic appears to be in that part of the Bachopi country lying in the angle formed by the Victoria Nile and the eastern shore of Lake Albert. In this area there have been a considerable number of deaths, which, from facts gathered by Dr. Pooley and from widely varying native reports, I should judge already amount to several hundreds. An estimate is rendered more difficult, if persistent native reports are to be believed, by the co-existence, during the last year or so, of small local epidemics in the same area of an acute and rapidly fatal disease, called by the Bachopi "kituli," which appears to be the same as the Luganda "kaumpuli," and is probably plague.

There are no reliable data available to show how long the sleeping sickness epidemic has been going on, but, calculating from the alleged number of deaths and the proportion of sick who have been seen in a late stage of the disease, it would appear that it has lasted at least a year, probably more. No evidence is obtainable as to how the infection first reached this epidemic area, but the probabilities of the case will be referred to later on.

Sleeping sickness was not found to be present as an epidemic anywhere along the route followed, which included the places mentioned above and extended to a point about ten miles west of Fajao in the direction of Bugungu. A few isolated cases were seen at widely distant points.

I was, unfortunately, prevented by want of transport, my porters being worn out, from traversing the country in the angle formed by the Victoria and White Nile, where, from what I have learned of the nature of the country and its population, I thought the disease likely to spread, but I visited part of this district on the bank of the White Nile by steamer later.

Glossina palpalis was found to be widely distributed on the Nile and lesser streams, and facts were gathered as to its local distribution and habits. The conditions favourable to the spread of sleeping sickness exist over a much wider area than the epidemic itself, as will be shown. They seem nowhere, however, unless perhaps on the shores of Lake Albert, favourable to the occurrence of a great epidemic such as that on Victoria Nyanza.

With regard to preventive measures, no complete system of quarantine or isolation would be possible owing to the characteristics of the disease itself, and if attempted would paralyse traffic and transport over a great part of the Protectorate and elsewhere. The prospects of destroying the fly to any useful extent is apparently hopeless. The measure which will be recommended as most likely to be effective and most generally practicable is a form of local and partial segregation which can be carried out by the natives themselves, and which consists in removing sick and suspected persons from communication with the neighbouring area or areas infested by fly.

II.—*Enquiry into the Presence of Sleeping Sickness.*

Great difficulty was experienced everywhere north of Masindi in gaining any assistance or reliable information from the natives, who have had little to do with Europeans and who were found to be extremely shy and suspicious and much prejudiced against showing their sick, their time-honoured custom being to hide them away in the jungle on the approach of strangers. They invariably denied all knowledge of the disease or of its presence in their country, except that, in a few instances among the Bachopi, they said they had heard of its presence at Mwanga's (Bugungu). They had, or professed to have, no name for it. It is perhaps worth noting here that I never found a sick person of any kind in a village in which it had become known that I was in search of sleeping sickness. There was great difficulty, also among the Bachopi in getting interpreters, as these people seem to have mixed very little with Baganda or Swahilis and generally knew only a few words of Sudanese, if any.

One could, therefore, form a judgment as to the presence of an epidemic only on general grounds, such as the general health and condition of the people, the state of the villages, gardens, etc., and the presence of recent graves. It can be stated with practical certainty, however, that, along the route followed by the expedition, excepting possibly the neighbourhood of the Waiga River, which will be again referred to when speaking of plague, sleeping sickness was not present in epidemic form, though isolated cases, if they existed, might easily have been concealed.

Having heard that there was, or had been, an epidemic of some kind near Kiswata's, on the Masindi-Fajao road, I obtained an interview with Rubangu, the chief of that district, at Masindi, in which he promised to collect the sick for me at the Waiga River camp, which is near there, and to provide guides. When I arrived, however, I found that nothing had been done and I could obtain no guides who would tell me in what direction the sick people lay. I was told on my arrival that all the sick people, five in number, had died the day before. After waiting two days, however, a woman was brought to me in a moderately advanced stage of sleeping sickness. She had general superficial glandular swelling, and gland-puncture in the neck revealed the presence of *Trypanosoma*. I could find no other cases, however, and the people there denied all knowledge of sleeping sickness, though they circumstantially described a recent epidemic of what they, the Bachopi, call "kituli," which is probably plague, and which they said had now disappeared. The woman just mentioned was stated to have frequently visited Lake Albert, near the mouth of the Waiga, and to have also been to Mwanga's (Bugungu), but it was also said that she had only been ill five days.

Between this and Fajao the population near the road is very scanty and I could find no case in which there was any suspicion of sleeping sickness, while at Fajao itself, which appears to be only too well adapted to the spread of the disease, the natives denied all knowledge of it, and I could find no sign of its presence. Enlarged glands were not common, but three cases were tested by gland-puncture with negative result. From Fajao to Foweire the conditions are less favourable to the spread of the infection, and here again all knowledge of the disease was denied. Enlarged glands were comparatively uncommon, and though several cases were tested by gland-puncture in various villages, in all eleven, the results were in each case negative.

Between Fajao and Wadelai I saw no natives, as they all ran away and did not even sell food to the porters. Between Lake Albert and Wadelai, near the former, on the Bank of the White Nile, at a village called Kobo's or Buba's, I saw one man with well-advanced sleeping sickness, having muscular tremor and enlarged glands. Not only, however, would he not allow me to examine his glands by puncture, but he refused even to put out his tongue. I saw one child in the same village whose condition was very suspicious, but any attempt to examine it gave much alarm, and I saw no more cases.

The natives north of the Victoria Nile appear to be afraid of witchcraft, and regard all European medicine as magic. At a village in the Bari country they said: "you would not go to see a man performing the calls of Nature, why should you want to look at him when he is sick?" so that in some cases they appear to be ashamed of being ill.

At Wadelai, Dr. Strathairn told me that Capt. Greig had found trypanosomes by gland-puncture in one of the police, and

he showed me a Uganda woman who seemed to be in an early stage of sleeping sickness, though a single gland-puncture in the latter case gave negative results. It is probable that the infection was not contracted locally in either of these cases, but they are of interest in considering the origin of the infection of Lake Albert and the Nile Valley.

At Kerris, half-way between Gondokoro and Nimule, I heard that there was a sick woman in a village, but on visiting it had great difficulty in seeing her, and was at last permitted to do so only on promising to abstain from medical or surgical interference. I was therefore unable to test by gland-puncture, but she was evidently in the last stage of sleeping sickness, and had been many months ill. She had been brought there from Nimule, where she was taken ill, and where, it was stated, other cases exist among the natives. She was alleged to have always lived at Nimule or Afuddu, and in that neighbourhood, and never to have visited Uganda or Unyoro.

I found no sign of the presence of sleeping sickness north of this.

III.—*The Fly.*

Glossina palpalis was not observed until the Waiga River was reached, where it was seen in small numbers at the point where the road crosses the river. It was afterwards found on so many of the streams encountered (unless where the channels were completely dry) that it is probably present on most or all of them wherever and whenever the conditions are favourable to it. It was, however, very scarce on the smaller streams, and often difficult to find. On the Victoria Nile it was numerous on both banks at all the points visited, and is probably practically continuous along the river as far as the rapids extend. On the White Nile it was numerous on both banks wherever the conditions seemed to favour its presence, but its distribution was more patchy. It was not found on either bank at Wadelai itself, nor between that place and Nimule, but at the latter locality it is again plentiful. It was also found at various points further down on the Nile. The furthest point north at which it was met with was near a small stream about 35 miles south of Gondokoro, between Kanda and Shindiro. It was seen on most of the streams further south.

It is probable that *Glossina palpalis* is present on all streams and open water where certain conditions prevail, viz., open water with shade, and a certain amount of clear beach, bank, or rock. Thus, on the Victoria Nile, which presents much the same features between Fajao and Foweire as the same river in Busoga—namely, high cliff-like banks covered with rock and scrub overhanging running water—the fly is extremely abundant. On the Nile from Lake Albert to Wadelai the conditions are more varied, but wherever the bank was fairly clear of close high reeds, swamp, or sudd, and was moderately shaded by jungle or even small scrub, the fly was always found. Where

the bank was free of reeds, sudd, jungle, or scrub the fly was rare or absent. Behind a wide expanse of close high reeds, swamp, or sudd, even if there was shade along the coast itself, the fly was also rare or absent; but it does not seem to mind open reeds, weeds, or rushes, or a narrow belt of swamp. As the above sets of condition may be said, roughly, to alternate with the curves of the river on the banks of the Nile at this part, the fly may be imagined as distributed in a line which zigzags irregularly across the river. At Wadelai, however, and from there to Nimule, with much sudd and swamp on both sides, only a little clear bank, and rarely shade at the same time, the fly was not found. At Nimule again, where there is shade without swamp, and north of it more or less clear banks owing to the rapids, the fly was found at several points. It is probably present wherever there is a belt of shade. In the immediate vicinity of Gondokoro, where there is no shade there is no fly. On the lesser streams and rivers the fly was generally in small numbers only. The conditions determining its presence there are similar to those of the main river. Where the stream is very narrow, high grass appears to give sufficient shade, and high perpendicular banks are also always favourable. The fly was found to be fairly abundant at some waterholes left in the dry beds of streams, being probably concentrated at places where water remained. It was not met with along channels which were entirely dry, nor was it seen at swamps or waterholes apart from streams.

There is in reality no continuous fly-belt, and, though it has been customary to use the term as referring to the range of the fly from a given piece of water, it will probably be found more convenient to reserve it to determine the geographical distribution of the fly across the continent of Africa. What is found locally is rather a series of patches on lake or riverside which may or may not be continuous.

The range of the fly from the water side is probably much narrower than has been supposed. Only on a very few occasions was it seen in ones or twos at any distance from water. The outside limit may be given as 300 yards, but seldom exceeds 50 or 100 yards. Probably on all the occasions on which the fly was found at a distance from water it was following the caravan; in fact, as was early noted, it will follow people from water to a certain distance till it has fed or been driven off. It was never met with while approaching water at any distance from it. Although I often camped at 100 or 200 yards from water where the fly existed, I only on one occasion found a fly in camp, and this had evidently followed the water carriers. In the camp at Fajao, where I spent altogether on two occasions nearly three days, I never saw a fly, though the tents were pitched close to the river on a high cliff beneath which the fly was to be seen in great numbers, and I had offered a reward to the porters for each fly caught away from the water side. It is

possible that the range of the fly may be increased in thick forest or in wet, cloudy weather, but this I had no opportunity of testing.

It was noted that *Glossina palpalis* will come freely to a boat off shore at a distance of about 30 yards or less but rarely at a greater distance. It will remain on board for a long time and may be carried for at least several miles. It does not begin to bite, as a rule, till the sun is well up, and it is difficult to be found half an hour before sundown. The surest way to detect its presence is to sit down close to the water's edge and wait, either in the shade or in a small open space. It may sometimes be necessary to remain half an hour or an hour or even more before seeing one, and it is well to have one or two natives sitting or standing in front of the observer. After a little experience the fly's presence may usually be detected by the ear before it is seen. It prefers to settle near the ground, especially on the under parts of the body such as the bends of the knees and backs of the calves when one is in the sitting posture.

The Bangoro call biting flies "bwara" if large, and "kiwara" or "kivara" if small, but appear to have no special name for the tsetse flies. The Bachopi call the tsetses "malingwa." They say that *Glossina palpalis* "follows the hippopotami," but it was found in many places where these animals seldom or never come, and was absent from others where they abound. The natives north of the Victoria Nile use the term "buda," which is applied by the Sudanese to any insect which bites by piercing, including mosquitoes. The tsetse is sometimes called "buda kebir." Several chiefs near whose villages the fly was found said they had never seen it before, though it seems that some of them, at any rate, had been shown it by the Collector of this district. The specimens of biting flies collected by me have already been sent in.

IV.—General considerations.

The following facts and conclusions seem to me to be of chief importance for consideration in dealing with sleeping sickness:—

1. The infection (trypanosome) can be carried from person to person only by the infected fly, and from place to place only by infected persons, via the infected fly.

2. If, as is stated, *Glossina palpalis* can carry the infection only for 48 hours or so, the risk of its conveying it to human beings in a given area must vary extremely according to the number of people in it or visiting it, the number of flies and the frequency of their opportunities for biting the sick. The scarcity of trypanosomes in the peripheral blood of the sick diminishes the probability of the fly acquiring or conveying the infection by any one bite, and so emphasises the importance of decreasing its opportunities as much as possible. The fly soon ceases to be a danger unless constantly re-infected.

3. The human being, on the other hand, may carry the infection for many months and possibly for years, and is a

constant source of danger so long as he is in or communicating with the fly-range. If kept from contact with the fly, however, he is harmless.

4. The range of the fly from water is very narrow, probably less than a quarter of a mile, and usually much less.

5. The risk of infection is at its maximum in a community or village situated within the fly-range, for there the sick people constantly re-infect the flies, and a village partly within the fly-range is practically in the same case. Between villages situated within a fly-range or ranges there is reciprocal infectiveness. This is particularly noticeable along lake shores and navigable rivers and among islands.

A village, the greater part of whose population is employed daily within the fly-range, as in fishing or canoeing, is almost in the same case with one lying within the fly-range, with the important exception that, in the later stages of the disease, when the sick are peculiarly at the mercy of biting insects, they no longer visit the water-side.

6. Such villages as those mentioned above are of especial danger on a line of frequent communication.

7. In a village whose inhabitants visit the fly-range only for drawing water or for ablution the risks are greatly diminished.

8. In a village away from the fly-range a great part of the population may become independently infected, and the risk varies with the distance from the fly-range and the frequency of communication with it. It is greatly increased in certain situations, such as on peninsulas or islands and between rivers (*See* Figs. I, II, and III). In such villages the able-bodied are the most liable to infection and are usually the first attacked. Infection cannot be carried directly from such a village to another outside the fly-range, but can only travel *viâ* the fly-range.

9. Infection is carried from place to place by man and not by the fly, though an infected fly might conceivably be carried for a considerable distance artificially, *e.g.*, on a steamer. It is evident that persons in the early stage of trypanosomiasis may carry infection to great distances, while the range of the individual fly is narrow and the period during which it carries infection is short. It is probable, therefore, that fresh areas become infected *viâ* the main routes of communication, rather than from more or less adjacent fly-infested belts or patches through which there is little or less communication.

10. The risk of infection being carried from one place to another depends then, chiefly, on the amount and character of the communication between them. The greatest risk is run when this is entirely or principally within the fly-range, as it commonly is along lake shores and navigable rivers. The most marked example is to be seen in the canoe traffic of the natives, in which the course is, wherever possible, in-shore, and the landing-places are frequent and generally uncleared. The danger is

comparatively slight of the infection travelling along or across unnavigable rivers, such as those parts of the Nile where there are rapids, and is determined more by the extent of road-communication than by the river itself and the number of flies on its banks. The risk from an infected person travelling depends on the number and character of the fly-infested areas crossed and, especially, on the time spent in them. It is obviously greatest when an infected person settles, or remains for some length of time, in or in close communication with an infectable area.

11. The conditions necessary for the occurrence of a great epidemic may be stated as follows:—

- (1.) The presence of *Glossina palpalis* in large numbers over a considerable area.
- (2.) A thickly-gathered numerous population.
- (3.) Free and frequent inter-communication, much of it within the fly-range.
- (4.) A considerable part of the population either living or daily employed within the fly-range.
- (5.) A coast or banks much broken by inlets, estuaries, and rivers, and with adjacent islands.

These conditions may be summed up as the constant infection and re-infection of large numbers of flies and the exposure to them of large numbers of people. They will be comparatively rarely found to co-exist in such fatal completeness as they do round the northern shores of Victoria Nyanza.

V.—*Preventive and Precautionary Measures.*

Sleeping sickness, then, may be carried wherever an infected person travels—a possibility which is practically unlimited. The disease may spread and find new victims wherever *Glossina palpalis* exists—a very wide field indeed. The chances of its spreading locally will, however, vary with certain conditions, such as the number of flies, the number and habits of the population, the location of their dwellings, the amount and kind of inter-communication and the conformation of the country. Most of the preventive measures used to combat other epidemic diseases are inapplicable in dealing with this terrible and fatal malady, and the difficulties to be overcome in carrying out any measure efficiently are enormously increased, not only by the special characters of the disease itself but also by the nature of the countries and populations where it is prevalent.

Quarantine, properly speaking, is impossible, owing to the great length of time during which infection may be carried by human beings and the difficulty of determining its presence in the early stages.

Aggregation of the sick for isolation purposes in large numbers is attended with great difficulties and drawbacks, and has no special advantages. Such aggregation within the fly-range must of course be harmful,

The difficulties in the way of quarantine preclude the feasibility of preventing the infection from being occasionally conveyed, wherever there is communication, to a new infectable area, and, though this may be controlled to some extent, it would seem that greater success is to be hoped for in endeavouring to limit the infection of flies in new areas and their re-infection in epidemic areas so as to reduce the risks to or from residents or travellers in each locality as far as possible.

The most practical method of accomplishing this result would be the removal of the sick in each community from direct communication with the neighbouring fly-range. This range being generally very narrow, the purpose would be effected in most cases by moving the infected patients to the next hill or open space, which need not be more than half an hour from the water-side. They would have to be supplied with water and sometimes, but not necessarily or always, with food as well, by their neighbours. This plan would of course be more difficult in a district in which a large proportion of the population had already contracted the disease. The chief difficulty will always be with cases of early infection. If, however, this plan were only partially carried out it would enormously decrease the risks incurred by the constant re-infection of flies. Where it could be carried out thoroughly it would stamp out the disease, and it should be enforced primarily at camps and villages on the main lines of communication.

It is probable that the natives, though generally reluctant and suspicious of anything new, would not have the same prejudices against such a measure as they have against complete isolation and removal to a distance from their homes and friends. Chiefs and others in districts where the infection exists or is likely to penetrate should be shown specimens of the fly and instructed as to its habits and how it carries infection, and special stress should be laid on the fact that only when it is allowed to bite the sick does it convey the disease to others. They should also be given some idea of the course and duration of sleeping sickness, and warned as to the early attacks of fever. They could then be instructed to remove all sick and suspected persons to a distance half an hour from any water where the fly is, to prevent them from visiting such water and to see that their friends supply them with water and food. They should report the appearance of cases of sleeping sickness in their district as they occur. Where feasible whole camps or villages could be removed from within the fly-range. In villages outside the fly-range it would only be necessary to prevent the sick from direct communication with it.

Instructions similar to the above were given to the chiefs at villages through which I passed. These men seemed quite willing in most cases to carry them out for their own sakes, if occasion arose, and did not suggest any difficulties in the way. With the support of the administrative authorities I think that

FIG II.

DIAGRAM OF THE PROBABLE MODE OF
EXTENSION OF SLEEPING-SICKNESS IN
BUGANDA & BUSOGA
EPIDEMIC A.

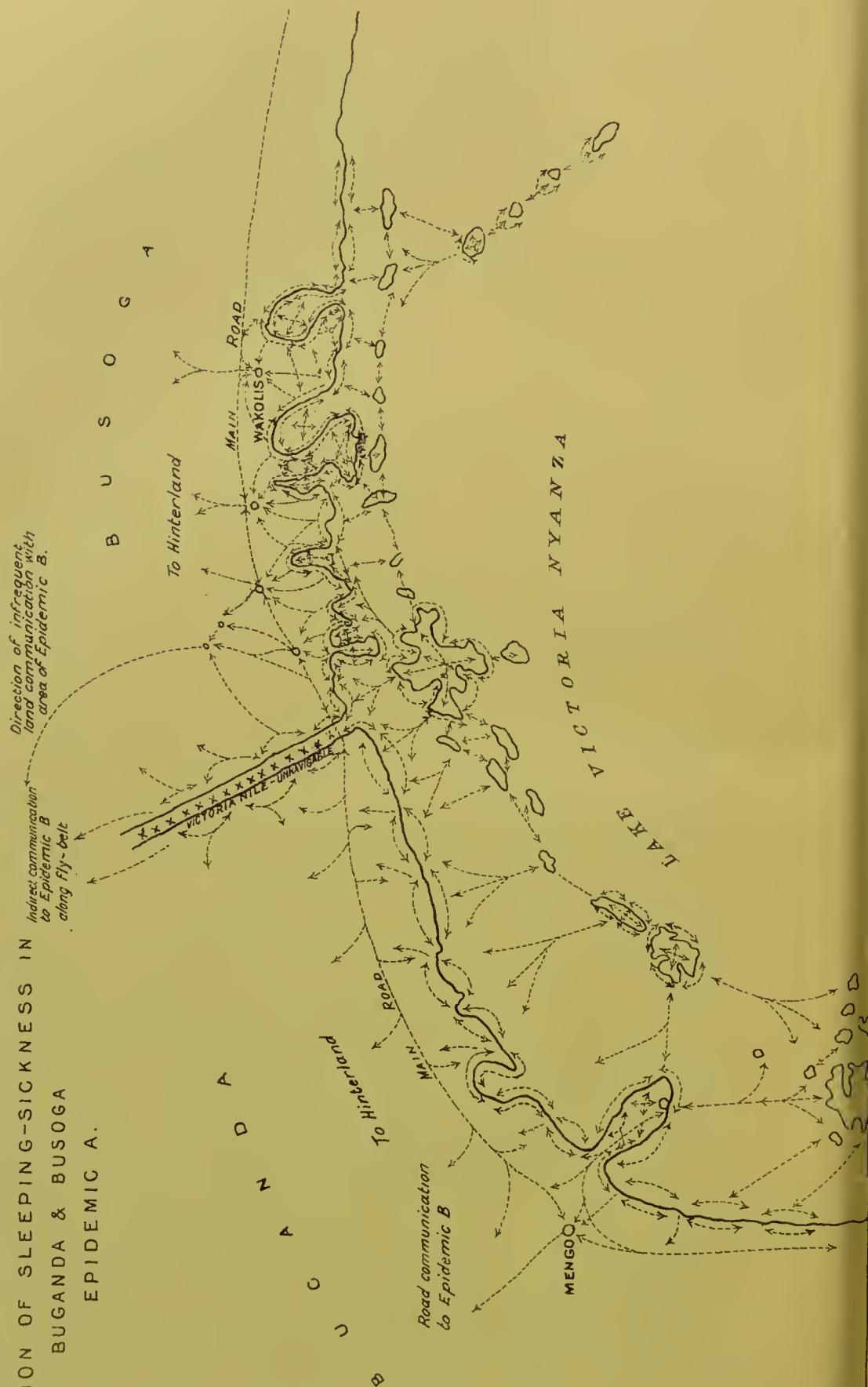
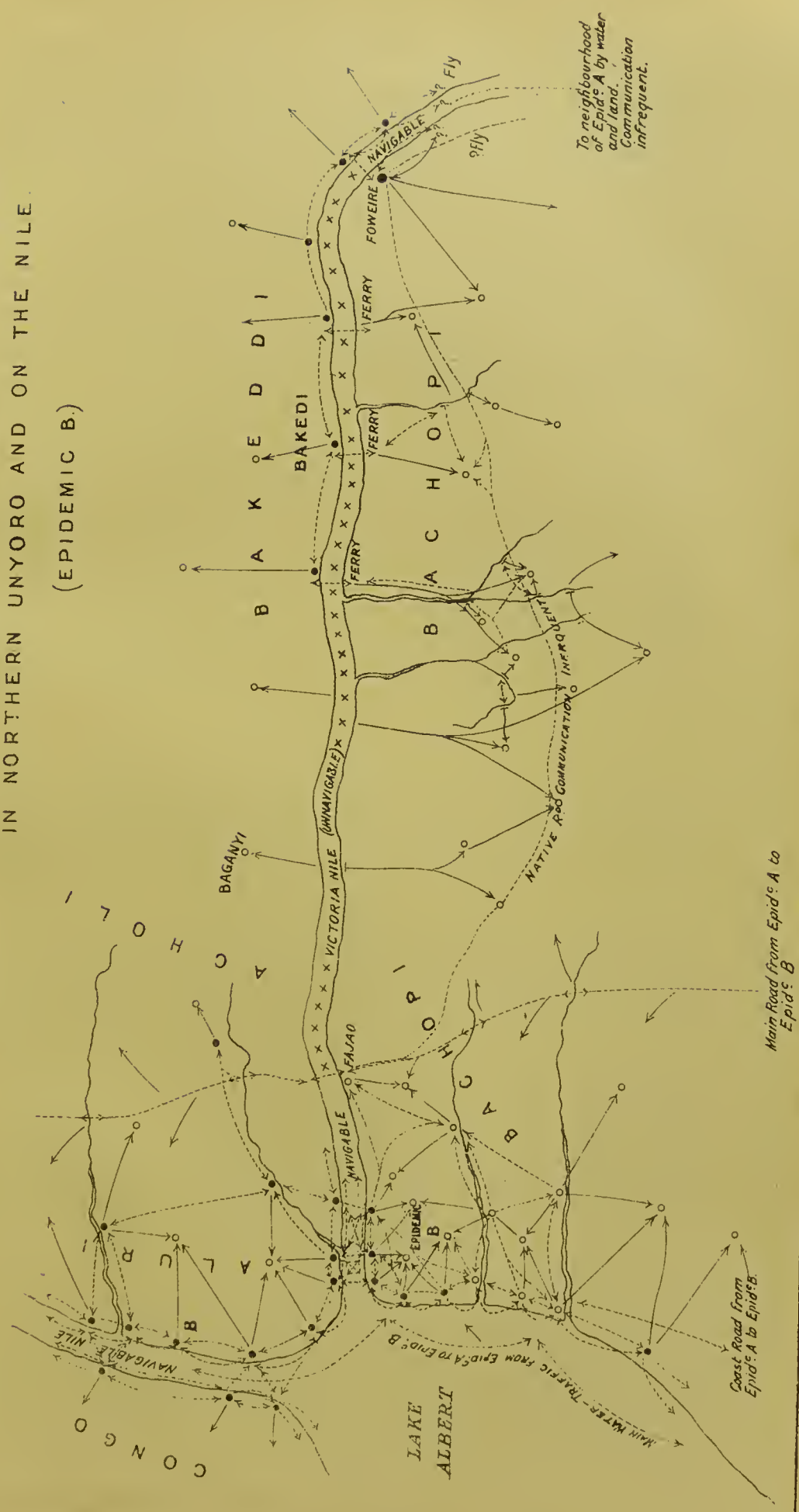


FIG. III.

DIAGRAM SHOWING CONDITIONS OF
POSSIBLE SPREAD OF SLEEPING-SICKNESS
IN NORTHERN UNYORO AND ON THE NILE.

(EPIDEMIC B.)



many of them would do their best to follow any such instructions given them. Where chiefs are found unwilling or incapable it might perhaps be possible to find Baganda, familiar with the disease, who could be employed, in some parts of the country, as native inspectors, and would see the instructions carried out.

Precautionary measures such as the medical examination of those travelling from an infected to an infectable area should of course not be neglected. Persons having glandular enlargement might be tested by puncture. People from an infected area should not be allowed to settle for any length of time in an infectable area without medical examination and special permission, and, when such permission is granted, should report themselves periodically.

Camps for transport purposes should not be nearer than 200 yards, and where possible 400 yards, from the water, and the ground near crossings and places where water is drawn should be kept well cleared of scrub. Where it is absolutely necessary to have camps near the water-side the sites should be carefully chosen and prepared. Water traffic should be conducted where possible at least 50 yards from shores or banks likely to harbour the fly, and landing-places should be chosen at spots which it is not likely to haunt.

The actual manner in which sleeping sickness spreads is highly complex, owing to the peculiar distribution of the fly and the various ways in which it can be reacted on by human inter-communications and occupations, and by the conformation of the country.

The map diagrams accompanying this report are intended to demonstrate how infection probably spread in the Victoria Nyanza epidemic (Epidemic A, Fig. II) and how it may possibly extend in and from the Albert Nyanza epidemic (Epidemic B, Fig. III).

The coast lines are entirely diagrammatic. Lines with double arrow heads (\leftrightarrow) show how infection is carried in both directions between any two points within the fly-range or from one fly-range to another, and represent, what has been called above, reciprocal infectiveness. Lines with single arrow heads show infection travelling to points without the fly-range, and represent so-called imported cases.

In Fig. I, E = lake or navigable river; F = fly-range; A, B, C, D = villages within fly-range; a, a¹, a² and b, b¹, b² = villages outside fly-range. All cases or centres in A, B, C, D are reciprocally infective, while a, a¹, a² and b, b¹, b² can only infect one another through some infected point in F, and are not reciprocally infective with A, B, C, D. (Fig. I, *see* p. 99.)

In Fig. II an attempt has been made to show the influence of islands, peninsulas, &c., on intercommunication and reciprocal infectiveness, and also how certain communities, though outside the fly-range, may be so situated that the greater part of their population may be swept off in a great epidemic while they themselves cannot convey infection directly to other communities outside the fly-range. An instance of this is the place marked Wakolis.

In Fig. III, I have tried to show how sleeping sickness may be expected to spread in the Lake Albert epidemic, and I am persuaded that a fairly accurate forecast might be made were a more detailed knowledge of the country and its inhabitants available. For greater distinctions only the lines showing reciprocal infectiveness have been marked in red.

It will be seen that the conditions favourable to the occurrence of a major epidemic are present to a great extent on the N.E. shores of Lake Albert and on arms of the Nile near it. It is possible they may also exist at other parts of the lake shore. There are, however, several reasons which render unlikely an epidemic of anything like the dimensions of that about Lake Victoria, namely:—

1. There is nowhere such a large and thickly gathered population.
2. There is much less intercommunication and trade.
3. There is nowhere so large a proportion of the population following their daily avocations within the fly-range.
4. On the White Nile, at any rate, most of the dwellings seem to be situated outside the fly-range.
5. What I have been able to gather regarding the conformation of the coasts and banks and the number of islands leads me to believe that the country is less fitted for the spread of infection. Between Fowcire and Fajao nearly all the villages are some miles from the Nile, many of them draw water from springs and waterholes not directly connected with streams, and most of the others are at least half a mile from streams. The fly is scarce on these streams, communication is infrequent, and the inhabitants have practically no aquatic occupations. Of the Bakedi and others occupying the country to the north of the Victoria Nile I can say little, except that they appear to control both banks of the river and to engage to some extent in fishing.

Along the White Nile to Wadelai the population is comparatively thin. Between Wadelai and Nimule the fly is scarce or absent (it may, however, be present on the streams) and the population is also thin. North of Nimule the population is again scanty and the river is, of course, unnavigable, but the road

*inhabitant for
the partial
is of
villages*

touches it at many places. There is no native intercommunication in all this region comparable with that among the Baganda and Busoga.

It would seem, therefore, if the infection makes headway in either of these directions, that a series of village or minor epidemics is more likely to result than a major epidemic like that round Lake Victoria. MB

Other diseases met with were small-pox and relapsing or spirillum fever. A disease resembling plague was described by the natives as existing in Unyoro and in the Bari country north of Nimule. Only one case of small-pox was seen, a porter in a caravan coming from Uganda. This man was isolated by arrangement with the local chief of Fajao and afterwards passed on to Gondokoro. No further cases, so far as can be ascertained, resulted.

Spirillum fever was common in my caravan, and several cases were met with in native caravans encountered on the road. In all 21 cases were seen and verified by microscopic examination. This disease seems to be specially prevalent in Unyoro. No cases occurred north of the Victoria Nile which might not have been contracted south of it, and no case has been seen since arriving at Wadelai. The disease seems to be closely associated with the tick *Ornithodoros moubata*, and is therefore probably identical with the Zambesi "tick fever." Some interesting cases occurred among my own servants. On December 14th my servants complained to me that there were many of the ticks, called "Bibo" by the Baganda, in the rest huts at the camp where they had slept that night and the night before. They had previously slept in their tents and I ordered them to do so again in future. On the night of December 21 four of them were seized with sharp attacks of spirillum fever. As, so far as I and they could tell, there had been no further exposure to the tick (which is *Ornithodoros moubata*), these cases appear to throw some light on the causation and incubation period of spirillum fever. Only one of these four had a relapse, after an interval of 14 days. Relapses were not common in the other cases, and seems to be much less frequent in natives than in Europeans.

At Kiswata's, near the Waiga river, Mwechi, a "mukungu" there, told me that 6 months before my arrival 41 people had died in a shamba called Panyatoli of a disease which lasted from two to five and sometimes ten days. They had pain in the chest, stomach or neck and sometimes in the groins. Sometimes, also, they spat blood or passed it in the stools. This disease is called locally "kituli" and is apparently the same as "kaumpuli" in Luganda and probably identical with plague. Mwechi said he remembered it, in Kabarega's time, before the Europeans came, sweeping across the whole of Unyoro and killing many people. All who did not die left their shambas and villages and ran away. He had not noticed whether rats died. He said the

local epidemic was now finished, and I could not see a case, though five people were said to have died of some disease or other the day before my arrival.

At Kerri's, half way between Nimule and Gondokoro, I found a small village quite lately deserted and partially burnt, with at least one recent grave in it. A son or relative of Kerri who was with me at the time, told me that it had been deserted during the current month (February) on account of an illness of which two people had died, and which he described as lasting from two to five days with symptoms similar to those described above. The local name of this disease is "jeddr." At a neighbouring village, when I found a case of sleeping sickness, this story was denied, and my original informant seemed inclined to retract his story, but I rather think it was nevertheless true, as no other reason was vouchsafed for the desertion of the village. No case of malaria occurred among the natives in the caravan until Wadelai was reached.

APPENDIX TO DR. HODGES' REPORT ON SLEEPING SICKNESS IN NORTH-WESTERN UNYORO AND ON THE NILE.

Other Biting Flies.—In addition to *Glossina palpalis* several kinds of biting flies were noticed. Specimens of most of these have already been sent and they appear to consist mainly of Tabanidæ of various species and Simulium or sand-flies. The latter are found in quantity near the Nile, especially the Victoria Nile, but their distribution is very wide over Usoga, Uganda, Unyoro and the Nile Province. Tabanidæ are also widely distributed, but were seen in greatest numbers between the Victoria Nile and Wadelai. Biting midges (Ceratopogon?) were troublesome at Hairo camp, between Kampala and Hoima, and at various places along the Nile. They are about $\frac{1}{8}$ inch long, greyish, with small hairy spots on the wings. Unfortunately all the dry specimens collected, which included mosquitoes, midges, and some of the tsetse flies, were spoiled either by mould or putrefaction.

A tsetse fly, somewhat smaller than *Glossina palpalis* and of a more yellowish-brown colour, was seen at intervals along the native road from Foweire to Fajao. It seemed to be pretty widely scattered, but was nowhere numerous, and I found it difficult to catch. One specimen, which appeared to me identical with those I had seen, was caught by one of my servants on his neck, about five hours south-east of Fajao. This has already been sent in for identification. I next saw similar flies about two hours north of Fajao, near the Wadelai road, but failed to obtain a specimen, though, while trying to catch one which was settling on my putties, I was bitten by another on the back of the neck, the first intimation of the latter's presence being the peculiar buzzing noise which they make after feeding, and which was long ago described by Colonel David Bruce. I did not encounter them again till about half-way from Nimule to Gondokoro, where I saw and caught a single specimen, which I now send. Since arriving at Gondokoro, however, I have found them in considerable numbers at a spot about four hours east of the station, near the Kodweh (?) river. Here I succeeded in catching three specimens, which also I send herewith. I cannot, in the absence of any literature of reference venture to determine the species, but, from their small size and general coloration these flies seem most to resemble *G. morsitans*.

Trypanosomes in animals.—On January 6th, at a camp near Foweire, it was reported to me that one of some sheep I had brought with me from

Kampala seemed to be sick and could not keep up well with the caravan. As the weather was intensely hot and trying I was not surprised. I took the animal on the next day, when it was reported to be weaker, and it was carried for a short distance into camp, where, however, it immediately started feeding. I could detect nothing the matter with it but a very slight nasal discharge, but, as it could not keep up with us, I ordered it to be killed, previously taking a fresh specimen of its blood. In this I found two trypanosomes. I then took some dry films for staining, but by this time the state of the blood was unfavourable for microscopy and I found no trypanosomes in them. I also failed to find *Pyrosoma* or any other parasite. In the organs there were definite signs of disease, viz., pericardial effusion, and some petechial hæmorrhages beneath the pleura.

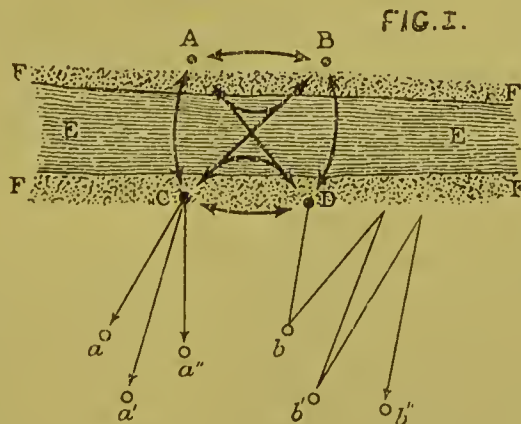
Soon after my arrival at Gondokoro I was informed that the Government mule used by the collector was ill. In its blood I found trypanosomes, and it died on March 2nd. At the *post-mortem* examination I detected nothing abnormal beyond anæmia and a few sub-pleural and sub-pericardial hæmorrhages. The brain was not examined. As the animal had been at the station three years the disease must have been contracted in this district.

ADDITIONAL NOTE BY DR. HODGES, DATED SEPTEMBER 6TH, 1905,
GONDOKORO.

The identification by an expert of the tsetse flies sent in with my report having confirmed my supposition that certain of these flies belonged to the species *Glossina morsitans* I am enabled to state now, what I suspected at the time, the fact that in every instance in which tsetse flies were caught at any considerable distance from water and from localities such as are described in the report as being affected by *G. palpalis*, the species has proved to be *G. morsitans*.

This would seem to be a somewhat important point in mapping out the distribution of *G. palpalis*, as it will be evidently rash to conclude that tsetse flies reported as existing away from localities such as described are of the species *palpalis*, unless specimens have been caught and examined with a view to the exclusion of other species.

Another fact brought into prominence is the very wide belt of distribution of *G. morsitans* across Africa, and this would seem to emphasise the importance of experiments as regards the ability of this species to carry the trypanosome of sleeping sickness, and thus to determine the potentiality of the spread of this disease to the many important areas where this fly is known to exist.



19. ACCOUNT OF TOUR BY MR. SPEKE AND DR. ADAMS IN NORTHERN UNYORO AND ON THE VICTORIA NILE.

BY DR. E. B. ADAMS.

(*November 14, 1905.*)

On September 8th, 1905, Mr. Speke and I started from Hoima on a tour through the Bugungu country to Fajao, thence along the south bank of the Nile to Fowera, and on to Buruli. We decided to abandon the last bit of the tour, and set out for Masindi when a day's journey above Fowera, owing to illness, and therefore did not quite reach Buruli.

2. For about ten days before starting on tour, we were employed in interviewing the different chiefs, through whose territory we should pass, and in showing them specimens of the tsetse fly and in talking to them about sleeping sickness. Mr. Wilson had also many talks with them, and had made them promise to cut tracks for us; if this had not been done it would have been almost impossible for us to have gone through the country which we did. The majority of them fulfilled their promises and cut roads for us and helped us considerably in other ways. The Kabaka also helped us by sending some of his headmen with us. These men were invaluable. The chiefs made one stipulation, and that was that no blood-films, &c., should be made. We took some time in explaining and showing them how they were made, but they insisted that if we once began collecting blood or gland preparations, we should find every village we came to deserted, and I have not the slightest doubt that this would have been the case, many of the natives running away as it was.

3. An itinerary of the villages passed during the tour will be found at the end. The tour was made in order to find out:—

- (1.) What places were infested by tsetse fly.
- (2.) In what places there had been cases of sleeping sickness, and whether the fly was found there as well.
- (3.) The nature of the locality in which the fly was found, and any habits of the fly.
- (4.) Whether sleeping sickness was increasing or decreasing in those places in which it was known to have occurred.
- (5.) If any means could be devised to prevent it spreading across the Victoria Nile by way of the ferry at Fajao, which is much used by traders, &c.

4. Our first camp was at Kajura, $4\frac{1}{2}$ to 5 hours from Hoima; no sleeping sickness there, nor could any fly be found. On the Wachi River there are only a very few natives, and those mostly

old people ; no cases of sleeping sickness. After prolonged search along banks of river two specimens of fly were caught, the only ones seen. There are very few there.

At Daudi's shamba there were also very few people. They said there had been no cases of sleeping sickness there. They knew the fly, but said there were very few there. I saw three only.

Musali's shamba.—No sleeping sickness ; a few flies were caught.

Henery's shamba.—No sleeping sickness ; two flies were caught.

At Bugaki there had been six deaths recently ; two of them were undoubtedly from pneumonia ; one came from Baramweli, possibly sleeping sickness. The other three might have been from sleeping sickness, but the native description of symptoms is not clear, and they undoubtedly conceal as much as possible. I saw one man who was ill. He was very thin and had enlarged gland in neck ; he permitted me to examine his blood—result negative. It was most probably an early case of sleeping sickness. Many flies were found there. This was close to the Weisoka River.

At Kitembe, close to the Hi-zi-zi River, which runs into the Waiga River, two days from Lake Albert, two flies were found close to the river, but there had been no sleeping sickness there and no deaths during the last year. During the last four months all their dogs had been dying. They had excessive diarrhoea and vomiting and great emaciation ; death in three to four months. They brought me one dog which was very thin ; I took blood-films—result negative. They said that all their puppies had been dying too. They brought me two which they had left. I bought one, which I took along with me ; blood examined, negative, and he is alive and fit up to the present time. Their goats and sheep were well. They had no cattle.

Matumbwa (headquarters of Mwanga), on the Zolia River. The Zolia River is close to the Waiga River, and runs into it just before the latter river runs into the lake.

5. The Waiga along both banks is infested with fly.

6. The following are the villages on the Zolia, in all of which sleeping sickness has occurred :—

Baramweli	7 deaths during last 3 months.
Matumbwa	5 " " " 3 "
Kitchwanti	5 " " " 3 "
Villages on the Waiga River :—			
Massegi	0 deaths during last 3 months.
Bnganna	0 " " " 3 "
Matumbwa	5 " " " 3 "
Kitagania	6 out of 12 died.
Kiriangandwa	12 " 30 "
Kiperi	12 " 25 "
Kiswata	All dead.

Mkondo	All ran away ; afraid of sleeping sickness or lions, probably sleeping sickness.	
Salizi	50	out of 60 died.
Kibamezi	5	" 20 "
Buseswa	25	" 40 "

One of the above places is put as being on two rivers ; it is between the two, and quite close to each of them.

7. It will be seen from the above list that there have been a considerable amount of deaths on the Waiga and Zolia Rivers. A good deal of trouble was taken in compiling the above list, different headmen being questioned and their answers being compared to what others had said. Mr. Speke interviewed them again and again, and I think that the above list is as accurate as it is possible to get from natives. I may mention here that we experienced considerable difficulty in getting reliable information from the chiefs and village headmen, and it was only after repeated interviews and questionings that we were able to arrive at any definite conclusions. They all appeared afraid of us at first, and tried to conceal as much as possible. "Sleeping sickness was always in the next village, but never in their own." But, by spending a good deal of time on them, I think we were able to overcome this prejudice or timidity to a very great extent.

Kinyambezu.—Eight deaths out of sixty, according to Mwanga. The headman denied it. Many flies. I saw seven undoubted cases of sleeping sickness.

Kakora.—Population about 100 ; five deaths during the last three months, two of them due to sleeping sickness ; one undoubted case there which I saw. The headman does not think that the cases were infected at home, but considers that the disease in each case was "brought from Bugungu" Very few flies.

Kipesi.—Population 18. Last three months four deaths. No sleeping sickness here. Zolia River about a mile away. The headman said he knew sleeping sickness very well, but that there never had been any in his village. No flies.

Muchunda.—Population 20. One death last three months, probably not sleeping sickness. Headman knew sleeping sickness ; no cases of illness there ; close to River Nsavia, which runs into Zolia.

Fajao (Okello's).—Population about 30. Okello states that there never has been any sleeping sickness in his village. He was most emphatic ; knows the flies, but states they are only found near the Nile ; I could find no sleeping sickness and no flies.

Fajao (ferry).—Kiza, the chief, stated that there was no sleeping sickness there and never had been, whereas Okello told me on more than one occasion that there were cases of sleeping sickness there. We found many flies, and the mosquitoes were very troublesome. Found no cases of sleeping sickness there,

though we searched the huts. Twenty men allowed me to examine the blood—result negative. I am convinced that there had been cases of sleeping sickness there, but we could find no signs of it, and Kiza most emphatically denied it.

8. We crossed over the river and found fly, but there were no natives there. We then proceeded down stream for two or three miles, and crossed the river; there was a small village about half a mile inland; no sleeping sickness. A few flies on river bank. Headman said he had never heard of sleeping sickness on that side of the river.

9. The inhabitants consisted of fishermen only, so it seems probable that if there had been cases, the infected men would have gone back to their own villages some miles away.

10. On leaving Fajao we went back to Okello's (Fajao), and did our best to get at the root of the matter, but could find no trace of the disease, in spite of several chiefs having repeatedly told us that there were cases there. After leaving Okello's we went to Buyayi, following up the course of the Victoria Nile, but some few miles inland; we were unable to keep along the river bank, owing to the nature of the ground, and the rapids prevented one using canoes. Two rivers were crossed, on the banks of each of which fly was found. The people of Buyayi fetch their water from the Nile as well, and flies were found there, and on the opposite bank no sleeping sickness.

11. At Tanyatiki, our next camp, flies were found; several sick men were examined, but there was no evidence of sleeping sickness.

12. At Gobo we heard the old story of white men killing and eating the natives. The latter, or many of them, evidently believing if a man died in the hospital he was killed and eaten by the Medical Officer in charge. They also in some way connect vaccination with the same idea. The Collector at Hoima informed me that it was difficult to procure labour on that account. We questioned them considerably about this matter, and eventually they brought up a very old man who admitted that he himself had been teaching this doctrine among his own and neighbouring villages. About a year ago a medical officer had been through the old man's village and had found his wife very sick. The medical officer had the woman carried back to the hospital, and in due course sent her back to her husband in good health; on the natives asking why the woman had not died at the hospital and been eaten, the reply was, that she was too fat or too thin. I think there is no doubt that the majority of the natives in that district (Chiopi country) "honestly" believe these stories, even proof like the above failing to shake their belief. From this it will be seen that it is not easy to get at the root *re* sleeping sickness. A few flies, no sleeping sickness and no deaths recently at Gobo. At this place again, we heard that there were cases of sleeping sickness at

Okello's (Fajao) and at the ferry. Mr. Speke at once doubled back, and by making forced marches at night reached Okello's early in the morning, obviously taking the people by surprise. The huts were searched systematically, but no sleeping sickness cases were found. They had evidently removed them some way inland or across the river, and had not yet brought them back. At Tyaki flies were found. The natives denied having had sleeping sickness there. Six sick men were examined by me; one of them might have been an early case of sleeping sickness; glands in part of neck slightly enlarged; very emaciated; no other signs. No deaths during the last year.

Todi.—A few flies; no sleeping sickness; no deaths.

Tanatwaba.—No flies; people all run away.

Powera.—No flies at first; on third day caught eight.

Koki.—No flies; no case of sleeping sickness at this place.

13. I was laid up with fever, and we decided to abandon the rest of tour and make our way back to Masindi. Nearly the whole of this journey was through low swampy ground; no flies were caught, and no history of sleeping sickness obtained. I had a slight attack of haemoglobinuric fever when about 35 miles from Masindi, and so did not reach there until October 28th, being carried in by Mr. Jervoise, Assistant Collector.

14. Regarding object of tour:—

(1.) What places were infected with fly?

(1.) See above.

(2.) In what places there had been sleeping sickness, and whether fly was found there as well?

(2.) Places and localities enumerated above for both sleeping sickness and fly; Kakoro being the only place where there was sleeping sickness and in which we were unable to find the fly. This may have been owing to the weather, the day being rather wet and overcast, unless it is more difficult to capture the flies; or it may be due, as the headman said, to the fact that the patients were infected elsewhere.

(3.) The nature of the locality in which the fly was found?

(3.) Always near water, within 250 yards, usually within 50 to 60 yards. A dry river bank with clumps of bushes, trees, and grass about; not as a rule if the grass was very dense, and no scrub. Where there were many trees and it was fairly dry, as in the forest below Fajao, they were plentiful. Where there was papyrus no flies were found near it; also they do not appear to like swampy ground. On the River Waiga there are plenty of flies, also on the Zolia, which runs into the above, but the latter river is swampy in part of its course; tall sword-grass and reeds: no flies were found here. On any of the

infested rivers, if they became at all swampy, no flies were found near by. The natives informed me that at this time of the year there are never very many flies to be found; many of them also told me that at times there are very many flies found in the swamps and around. Mr. Dawe, of Entebbe, also told me that he had seen them in numbers close by swamps, and that he had been "bitten" by them while crossing swampy places. I found them always on dry ground with bushes and trees, and also close to water. There are flies on both sides of the Nile below Fajao and above, but the further one gets from Fajao above, the less numerous the flies appear to get. At Fowera there were very few, and above that we found none. This is probably owing to there being more papyrus, and the banks becoming lower and consequently more swampy. There are not so many on the north bank. I think it quite probable that the flies do frequent this locality at certain times of the year. We never found them in banana plantations or in the native shambas. All small streams running into the Nile had fly on them.

- (4.) Whether sleeping sickness is on the increase or decrease in the Bugungu district?
 - (4.) This question is not easy to answer, as undoubtedly many cases were hidden. All the chiefs without exception stated that it was decreasing.
 - (5.) If any means could be devised to prevent its spreading across the Victoria Nile, by way of the ferry at Fajao?
 - (5.) A medical officer might be stationed at Fajao, to examine all caravans before they crossed, in order to stop any suspicious case. He would also be in a splendid position for noting habits and peculiarities of the fly, &c., &c.
-

20. REPORT ON THE ANATOMY OF THE TSETSE-FLY (*GLOSSINA PALPALIS*.)

By E. A. MINCHIN, M.A., Professor of Zoology and Comparative Anatomy in University College, London, late Fellow of Merton College, Oxford.

[Reprinted from the PROCEEDINGS OF THE ROYAL SOCIETY, Series B, Vol. 76.]

The following description is based upon dissections and preparations made in the laboratory of the Sleeping Sickness Commission at Entebbe since my arrival here at the beginning of April. I hope on my return to England to work up my material into a detailed memoir on the anatomy and histology. Time does not suffice for me to complete my work out here, but it seemed worth while, nevertheless, to bring forward as soon as possible a brief description of the general anatomy of the fly, and especially of its digestive tract, on account of its importance for the study of the evolution of the trypanosomes of sleeping sickness, and other tsetse-fly diseases, within the body of their invertebrate host.

In this paper I do not propose to attempt to deal with either the muscular system or the respiratory tracheal system. The former of these is so complex that much more time would be required for working it out than I could afford to spend, and it is, moreover, of little or no importance for the aim in view; while the tracheal system, or at least its finer branches, are so intimately connected with the fat-body, which here, as in other insects, fills up the body-cavity, that in the process of clearing up and laying bare the organs, the tracheæ are for the most part removed. Special muscles or tracheæ will be mentioned in places, but otherwise no account will be taken of these two systems.

The drawings illustrating this memoir are to be regarded as semidiagrammatic, but all details in them have been traced from sketches made with the camera lucida from actual dissections, and therefore claim to be true to nature and accurate as regards scale and proportions. For help in the preparation of these drawings I am much indebted to my colleague, Mr. F. Tulloch, R.A.M.C., who also kindly cut some sections for me. Mr. Tulloch has also made some dissections of *Stomoxys*, comparison with which has thrown light on some points in *Glossina*; Mr. E. Degen, who came out with me, has also helped me in various ways.

Since I have no access out here to any literature or works of reference dealing with insect-anatomy, I am unable to make this account comparative, or to state how far *Glossina* differs from other Diptera as regards internal structure. I shall content myself, therefore, with describing the facts observed by me in a purely objective manner.

In the following description I shall employ the term *waist* for the narrow peduncle connecting the thorax and abdomen, and *neck* for the still narrower connexion between head and thorax.

1. *The Nervous System of Glossina*, as of other Diptera, is concentrated into two masses, one situated in the head, the other in the thorax.

The brain (fig. 1) consists of the two large cerebral ganglia (*S. O. G.*) giving off laterally the still larger optic lobes (*Op. l.*), from which arise the optic nerves. The dissection of the brain and its nerves is rendered somewhat difficult by the large air-sacs, dilatations of the tracheal system, contained in the head. From the anterior side of the cerebral ganglia various nerves are given off: first, a medium nerve of moderate size to the three ocelli (*oc. n.*), arising from the furrow between the two cerebral ganglia, and apparently swelling out into a small ganglion; secondly, a pair of nerves to the antennae arising about half-way down the front of the brain on each side; thirdly, a pair of small nerves which innervate the muscles of the pharynx, arising near the base of the brain; and lastly, a pair of nerves to the proboscis, which arise from the base of the brain, run forward ventrally to the pharynx, giving off nerves at this point to the muscles of proboscis, and finally enter the bulb of the proboscis, to be distributed to the mouth-parts (fig. 5, *n. p.*).

From the posterior surface of the brain, near its base, the two stout connectives (fig. 1, *Cn.*) arise, and pass down on each side of the greatly narrowed oesophagus, after which they unite almost immediately to form a single broad band of nerve-tissue, which runs back through the neck to join the thoracic ganglion-complex. From this connective band, as it may be termed, there arises, immediately after it enters the thorax, a slender pair of nerves, which form a delicate plexus with the first pair of prothoracic nerves arising a short way behind them (fig. 1, *Cn. n.*).

The connective band often appears distinctly double at its junction posteriorly with the thoracic ganglion-mass, which lies immediately ventral to the proventriculus, the anterior end of the former being a short distance behind that of the latter. It is a mass of considerable thickness in the dorsoventral direction, and appears more or less pear-shaped in a dorsal view, but seen from the ventral side its anterior end appears truncate. When stained, cleared, and mounted in Canada balsam, it is seen distinctly to be composed of three pairs of large ganglia united

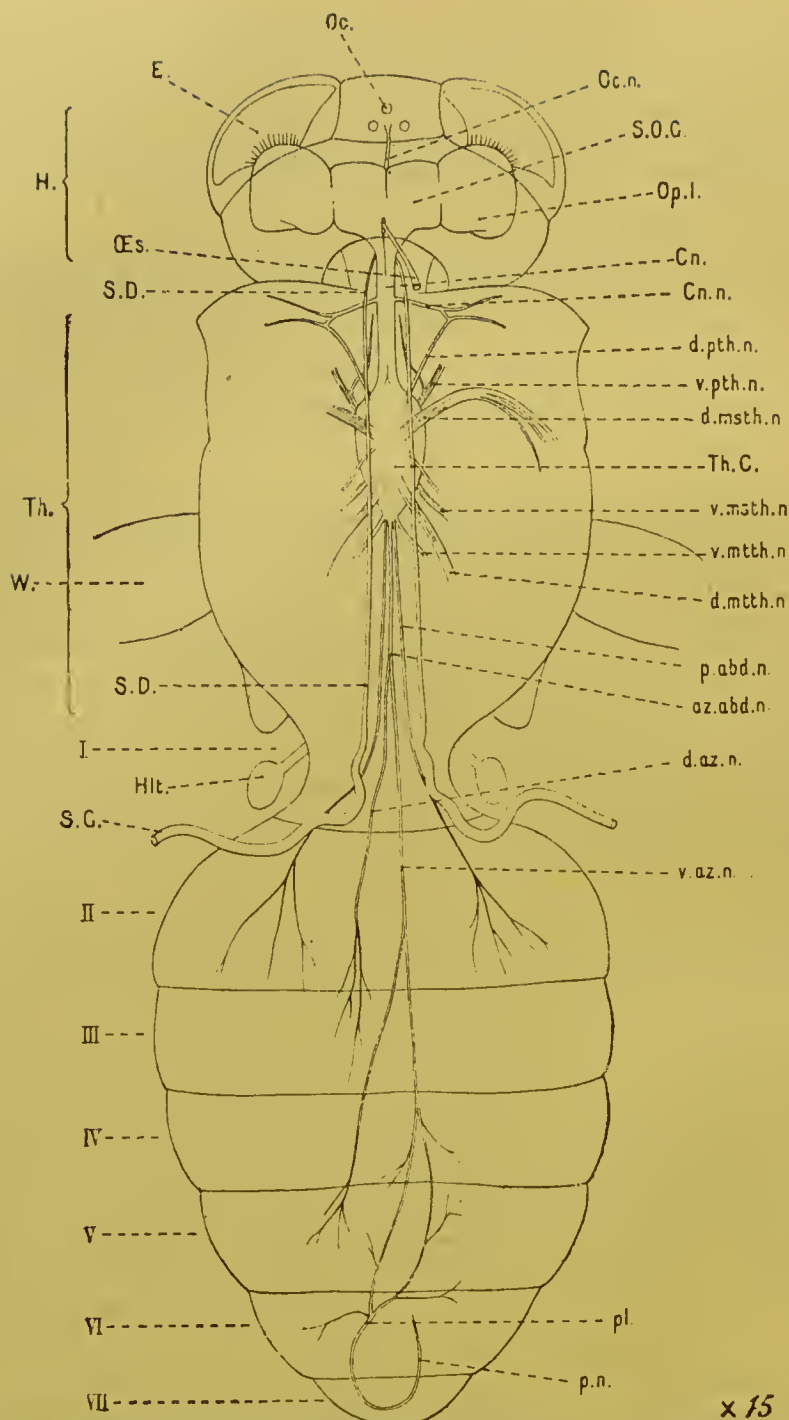


FIG. 1.—General Sketch of the Nervous System, dorsal view. The top of the head is pushed forward and downward as far as possible, to show the brain. A portion of the oesophagus and the salivary ducts are also represented, the salivary gland being supposed to be turned outwards from the abdomen and cut off near the origin of the ducts.

All lettering relating to the nervous system has been placed on the right of the figure, that referring to other parts on the left. *H.*, head; *Th.*, thorax; I—VII, the segments of the abdomen; *Oc.*, ocelli; *E.*, eyes; *Æs.*, oesophagus (cut off); *S. D.*, *S. D.*, salivary duct; *W.*, origin of wings; *Hlt.*, halter; *S. G.*, salivary gland; *Oc. n.*, ocellar nerve; *S. O. G.*, right cerebral ganglion; *Op. l.*, right optic lobe; *Cn.*, connectives; *Cn. n.*, nerve from the connective forming a plexus with: *d. pth. n.*, dorsal prothoracic nerve; *v. pth. n.*, ventral prothoracic nerve; *d. msth. n.*, *v. msth. n.*, dorsal and ventral mesothoracic nerves; *Th. c.*, thoracic ganglion complex; *d. mtth. n.*, *v. mtth. n.*, dorsal and ventral metathoracic nerves; *p. abd. n.*, paired abdominal nerve; *az. abd. n.*, azygos abdominal nerve; *d. az. n.*, dorsal branch of the azygos nerve; *v. az. n.*, ventral branch of the azygos nerve (genital nerve); *pl.*, plexus formed by the genital nerve; *p. n.*, nerve to penis.

together, corresponding to the three segments of the thorax, behind which a small mass of ganglion-cells, representing the abdominal nervous system, forms the posterior-pointed termination of the thoracic complex.

From each of the thoracic ganglionic centres arise two nerves, one dorsal and one ventral, so that altogether six pairs arise from the body of the thoracic complex, which are distributed to their proper regions of the thorax. From the posterior end of the thoracic complex arise three nerves, one medium unpaired, and two lateral paired, which pass backwards into the abdomen.

The greater part of the thorax of the fly is a mass of muscle, and as the muscles have to be removed in order to display the other organs in the thorax, the terminations and finer branches of the nerves are torn away from them. Hence it is impossible to describe accurately the destinations of these nerves without a detailed study of the musculature, which, as already stated, I have not made. It would appear, however, that the three ventral pairs of thoracic nerves innervate the legs and their muscles.

The dorsal prothoracic nerves (*fig. 1, d. pth. n.*) are very slender, and, as already stated, form anastomosis with the nerves from the connectives. The ventral prothoracic nerves (*v. pth. n.*) are of moderate size.

The dorsal mesothoracic nerves (*d. msth. n.*) are very large, being in fact the stoutest nerves in the body. They run slantingly forward, then curve round till they run in a backward direction, and appear to be distributed to the wing muscles. A small nerve arises from the ganglion close behind the origin of the dorsal mesothoracic nerves, and runs backwards in a dorsal direction. It is drawn in *fig. 1*, but not lettered, and is probably to be regarded as a branch of the dorsal mesothoracic nerve. The ventral mesothoracic nerves (*v. msth. n.*) are also of fairly large size.

The dorsal metathoracic nerves (*d. mtth. n.*) are large, the ventral ones (*v. mtth. n.*) of moderate size.

The three abdominal nerves run at first straight backwards, and almost parallel to each other, to the waist. Before reaching it the median nerve (*az. abd. n.*) has divided into a smaller dorsal and a larger ventral branch. After passing through the waist the two lateral nerves (*p. abd. n.*) diverge outwards to the sides of the abdomen and break up into numerous branches.

The dorsal branch of the median nerve is distributed to organs situated dorsally in the abdomen. The ventral branch of the median nerve is the nerve of the generative organs. In the male I have found that its branches unite to form a plexus (*fig. 1, pl.*) apparently containing a small ganglion, which gives

off nerves in various directions, and from which a fairly stout nerve (*p. n.*) arises and follows the ductus ejaculatorius in its tortuous course, till it finally enters with it the penis, the museles of which it innervates. In the female a similar plexus appears to be formed, but owing to the dense tangle formed by the fat-body, uterine glands, and Malpighian tubules, I have not succeeded in dissecting out its finer details.

2. *The Digestive Tract.*—Since the proboscis, buccal cavity, and pharynx have been thoroughly described in Austen's monograph by Hansen, whose account I can but confirm, I commence my description with the œsophagus. This portion of the alimentary canal (figs. 1 and 2, *Œs.*) runs first of all in an upward direction from the pharynx (*Ph.*), then bends sharply round and passes backwards through the brain. The first portion of the œsophagus is dilated, but slightly compressed, appearing of greater calibre in a dorsal than in a lateral view. After bending round, it narrows rapidly, and the portion which passes through the brain is of extreme tenuity, scarcely, if at all, of greater calibre than the salivary ducts. Behind the brain the œsophagus widens, at first very gradually, then, after entering the thorax, more rapidly, till it joins the proventriculus, into which it opens ventrally, breaking through the floor slightly in front of the point at which the thoracic intestine arises dorsally. From the point at which the œsophagus opens into the proventriculus, the duct of the sucking stomach arises.

The proventriculus, which marks the commencement of the mesenteron, has a peculiar and very characteristic form (fig. 2, *St.*). Seen from the dorsal aspect, it appears roughly oblong in form, with a bevelled anterior edge, and the upper surface more or less saddle-shaped, *i.e.*, convex in the transverse section, concave in the longitudinal direction. Seen from below, its lateral edges appear wrapped round the œsophagus and the duct of the sucking stomach, on which it rides, as it were. From the dorsal side of the proventriculus, about the middle of its length, arises the intestine, the first part of which (*Th. I.*) runs backwards through the thorax as a straight tube of even calibre, until it passes the waist. As soon as it enters the abdomen the intestine swells and becomes the strictly digestive portion of the alimentary canal.

The abdominal intestine is of great length, but until it reaches the proctodæum it cannot be divided into regions. It forms a number of complicated coils in the abdomen, and for purposes of description a number of limbs may be distinguished, each limb separated from the one next following by a more or less sharp bend (figs. 2 and 3).

The first limb (1) runs backwards along the abdomen in a dorsal situation, curving first slightly to the right, then more strongly to the left, until it reaches the fifth segment, where a sharp bend takes place forwards in a ventral direction. The

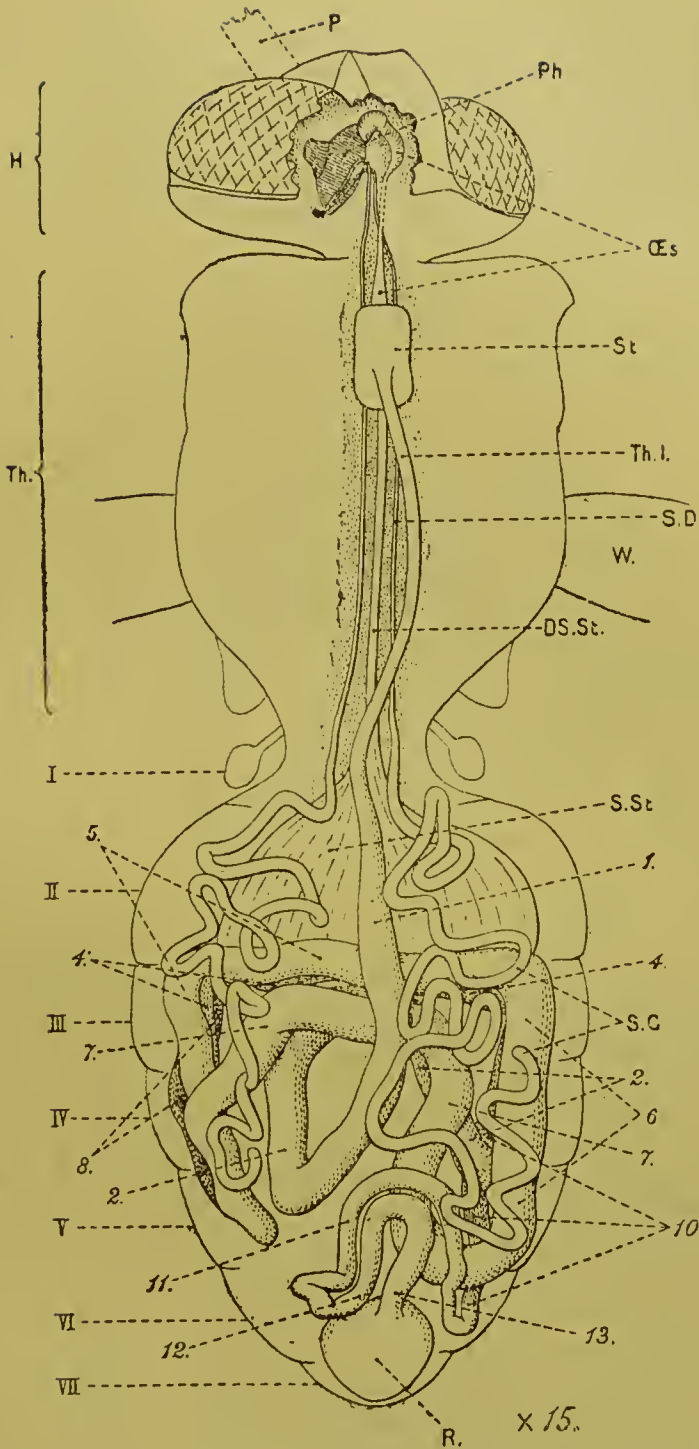


FIG. 2.—General View of the Digestive Tract, as seen in dorsal view without disturbing its parts. The heart and overlying tracheae and fat-body are removed in the abdomen, also the muscles in the thorax, and the brain and other parts of the nervous system are omitted from the drawing. The head is turned round to the left, in order to show the pharynx, etc., in three-quarter side view.

Ph., pharynx; *Œs.*, oesophagus (the portion which passes through the brain being represented with a dotted outline); *St.*, proventriculus; *Th. I.*, thoracic intestine, pulled over to the right, in order to show the duct of the sucking stomach lying beneath it; *S. D.*, salivary duct; *D. S. St.*, duct of; *S. St.*, the sucking stomach; *S. G.*, salivary gland (that on the right is drawn from a specimen in which the gland was more developed than in the case of that drawn on the left); 1–13, limbs of the abdominal intestine (see fig. 3); *R.*, Reectum. Other letters as in the preceding figure.

second limb (2) curves round from left to right, running first anteriorly, then transversely, and lastly in a posterior direction. It is more ventral in situation, being placed below some of the succeeding coils. The third limb (3) is short, and runs straight forward on the right side from the fifth to the third segment. Not visible in fig. 2, its position is indicated in fig. 3. The fourth limb (4) turns at right angles, and runs transversely across

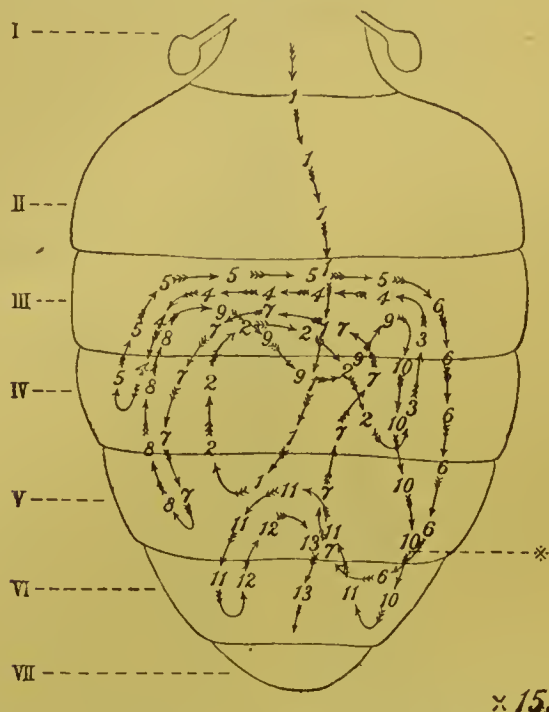


FIG. 3.—Diagram to show the various limbs (1–13) of the abdominal intestine, and their arrangement in the abdomen. The asterisk * denotes the point at which the Malpighian tubules arise in the tenth limb.

the body in the third segment, passing back a short distance into the fourth. The fifth limb (5) turns sharply back on the fourth and runs dorsally to it across the body again in the third segment. The sixth limb (6) turns back at a right angle and runs back on the right side of the body from the third to the sixth segment. The seventh limb (7) turns sharply forwards, then curves round in a roughly semi-circular course in the third segment, and finally runs backwards on the left side as far as the fifth segment. The fifth, sixth, and seventh limbs form together a well-marked loop, lying superficially, which is generally the most dilated portion of the intestine and represents the true stomach. The eighth limb (8) bends sharply forwards and downwards, and runs deep on the left side from the fifth to the third segment. The ninth limb (9) bends at right angles and runs at first transversely in the third segment, then curves back into the fourth, then forwards again into the third segment. The tenth limb (10) runs backwards along the right side of the body from the third to the sixth

segment, and in the fifth segment gives off the Malpighian tubules (*, fig. 3), so that from this point the gut must be regarded as proctodæum. The eleventh limb (11) runs from right to left in a semicircular curve occupying the fifth and sixth segments. From the origin of the Malpighian tubules to the end of the eleventh limb the gut is of small calibre, and may be called the ileum. The succeeding portion is thicker, and may be called the colon. It lies in the fifth and sixth segments, and forms the twelfth and thirteenth limbs (12, 13), both short and sharply bent one on the other. The ileum and colon lie dorsally in the body, and the colon passes into the capacious rectum (*R.*), which has four rectal glands (fig. 5, *r. gl.*) each supplied by a bunch of small tracheæ.

The appendages of the digestive tract are the salivary glands, the sucking stomach, and the Malpighian tubules.

The salivary glands (fig. 2, *S. G.*) commence, starting from their distal ends, as two long tubes, much coiled, and occupying a very superficial dorsal position in the abdomen on each side of the heart, above the alary muscles. Very transparent in the fresh condition, the salivary glands become glistening white in colour when put in alcohol. Only tracheæ and fat-body come between them and the dorsal body-wall. The coils of the tubes extend back as far as the fourth or fifth abdominal segment, but the distal extremity of the gland may lie further forward than this. With many twists and turns the tubes run forward to the waist and then pass into the thorax, at the same time diminishing rapidly in calibre, straightening out their coils, and descending to the ventral side of the body. From this point the salivary gland becomes the salivary duct (figs. 1 and 2, *S. D.*). The two ducts run a parallel course through the thorax, on a level with the duct of the sucking stomach, and on each side of it, passing under the proventriculus and above the thoracic ganglion (figs. 1 and 2). When they reach the neck, the salivary ducts become so extremely attenuated that their course through the head is very difficult to follow. As they enter the neck the ducts curve over towards each other, and pass under the connective nerve-band, thus parting company from the œsophagus, which passes above the connective. The ducts pass under the brain and then under the pharynx.

If the head of a fly be examined from below, there will be found, immediately behind the bulb of the proboscis, an area covered by soft flexible integument, which recalls the soft skin at the base of a parrot's beak, and has a similar function, that is to say, to allow free play for the movements of the proboscis. When the proboscis is bent down, in the attitude it assumes when the fly is drawing blood, the soft skin forms a fold over the bulb, and when the proboscis points forward, in the attitude of repose, enclosed in the sheath formed by the two palpi, then the soft integument is stretched. If this flexible skin be removed, a cavity

is exposed lying below the pharynx (fig. 4, *Ph.*) across which run the nerves to the proboscis (*n. p.*), a pair of retractor muscles

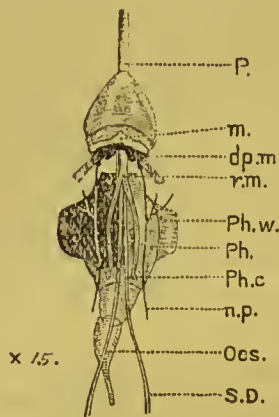


Fig. 4.—Dissection of Pharynx, Proboscis, Salivary Ducts, etc., ventral view.

P., proboscis; *m.*, soft integument cut away behind the bulb of the proboscis; *dp. m.*, depressor muscle of the proboscis; *r. m.*, retractor muscles; *Ph.*, pharynx; *Ph. w.*, chitinous wings of the pharynx; *Ph. c.*, membranous continuation of the ventral wall of the pharynx, to which the retractor muscles are attached; *n. p.*, nerve to the proboscis; *Æs.*, œsophagus; *S. D.*, salivary duct.

uniting anteriorly (*r. m.*) and the two delicate salivary ducts (*S. D.*). The last-named remain perfectly distinct and separated from one another until they pass dorsally to the median muscle formed by the two united retractors. A stained preparation, which I have cleared and mounted in Canada Balsam, shows the two ducts uniting into a single duct above this muscle. In *Stomoxys*, according to Hansen's description, the two salivary ducts unite into a median duct much further back than I have found to be the case in *Glossina*. Hansen, it may be noted in passing, speaks always of the thoracic salivary gland,* but in *Glossina* these glands are not thoracic, and in *Stomoxys* they are partly abdominal. The immensely powerful muscles of flight, filling up the thorax, are probably the cause of the glands being shifted back into the abdomen. To follow the further course of the salivary duct after it enters the proboscis, sections would be required, which I have not made, since Hansen has already described the duct as opening on the hypopharynx, as in all other insects.

The sucking stomach is morphologically a ventral diverticulum of the hinder end of the œsophagus, which is placed in the two anterior segments of the abdomen, its connection with the œsophagus being drawn out into a long slender duct traversing

* Austen also states ("Monograph," p. 35) that "the salivary gland [of Diptera] . . . is always situated in the *thorax*." (The italics are Austen's.)

the thorax. The sucking stomach in the ordinary condition of the fly is filled with gas, but shortly after feeding it is found filled with blood.

The duct of the sucking stomach arises, as already stated above, from the œsophagus, at the point at which the latter communicates with the proventriculus, in such a way as to appear as a direct continuation of the œsophagus, the opening into the proventriculus having rather the appearance of a dorsally-directed diverticulum. At the point where the communication with the proventriculus occurs, the sides of the proventriculus are folded down ventrally so as to wrap completely round the duct, meeting below it, and forming a complicated system of cavities into which the fat-body intrudes.

When the duct passes the waist, it expands rapidly to become the capacious sucking stomach (figs. 2 and 5, *S. St.*), which has delicate walls, provided with a layer of striped muscles disposed irregularly.

The Malpighian tubules (*M. t.*, *M. t.*, fig. 5) arise by a pair of main stems given off from opposite sides of the 10th limb of the abdominal intestine. Each of these stems very soon divides into two again. In *Glossina* these tubules are excessively long, and so entangled with the fat-body and other organs that it is impossible to unravel them for their whole length, but since they are never observed to branch again, after their origin from the two main stems, it may be inferred that, as in other Diptera, there are in all four Malpighian tubules, disposed in this case in two couples, each couple coming off from a common stem. When the dorsal integument of the abdomen is removed, it can generally be observed without difficulty that two of the Malpighian tubules have thickened terminations, which lie close alongside the heart in the pericardial sinus right and left. In some specimens of *Glossina* these two tubules are not conspicuously thickened, but their position is constant. In no case do they exceed the salivary glands in thickness. It is evident that these two tubules must be of physiological importance for purifying the blood in the pericardial sinus. Mr. Tulloch has found in *Stomoxys* the same two pericardial Malpighian tubules, thickened to such an extent as to greatly exceed in calibre the salivary glands. Mr. Tulloch also found, and I was able to confirm his observation, that the two pericardial tubules of *Stomoxys* were a couple, arising both from one of the two stems on one side of the gut. The Malpighian tubules being much shorter in *Stomoxys* than in *Glossina*, it was possible to dissect out the two pericardial tubules of the former as far as their common origin from the gut, at which point they were detached, stained, and mounted in Canada Balsam, thus putting this somewhat unexpected result beyond all doubt. Whether the two pericardial Malpighian tubules of *Glossina* are also, like those of *Stomoxys*, a couple with a common origin, cannot be stated with complete certainty, but it seems at least highly probable.

The morphological significance of this fact is, perhaps, that the two common stems of the Malpighian tubules are not to be considered as arising right and left from the gut, but as dorsal and ventral in origin. I have not succeeded in finding the distal extremities of the two remaining tubules, but they appear to pass down towards the ventral side of the abdomen and to be entangled with the genital organs, the dissection of which they help to render difficult.

3. *The Genital Organs* lie in both sexes close to the ventral side of the body in the hinder segments of the abdomen.

The male organs (fig. 5) consist of two pairs of tubes, greatly convoluted for a whole or a part of their course, which open all together into an unpaired tube, the ductus ejaculatorius, which in its turn passes to the external organs of generation and opens on the penis.

Commencing with the paired portions of the male apparatus, it is observed that the two tubes on either side differ markedly from one another. One pair, placed most posteriorly, is tightly wound and has the coiled portion pigmented. The other pair, more anterior, forms a looser coil and is without any pigment. I identify the former as the testes, the latter as the vesiculæ seminales.

Each testis commences with a delicate white filament (*t. f.*), embedded in the fat-body and difficult to trace. I have not succeeded in finding where the free end of the filament is attached; in dissections it appears to be loose. The filament passes on into the tightly coiled pigmented tube, which forms a conspicuous, compact, brown body, the testis (*T.*). In one dissection I succeeded accidentally in uncoiling the testis by pulling inadvertently on the filament when trying to remove the fat-body. It was then seen that each testis is a whitish coiled tube enveloped in a pigmented brown coat, which crumbles easily into a brown powder. In specimens that have been long in alcohol also the pigmented coat often sticks to the surrounding fat-body and comes away from the testis. The proximal part of the testicular tube is dilated and forms the testis proper; the distal portion is of smaller calibre and more tightly coiled, forming an epididymis, from which the tube is continued as the vas deferens (*V. d.*). The latter is a white, straight, or but slightly sinuous tube. The brown pigment of the testis is continued a very short way down the vas deferens, and ends abruptly.

Each vesicula seminalis (*V. s.*) is a white tube, commencing with a blind end. A short distance from the commencement the tube is slightly thickened for a short distance. There is nothing to bind the coils together, nor any pigment, as in the testis. Distally the tube straightens out to open into the unpaired duct of the generative system.

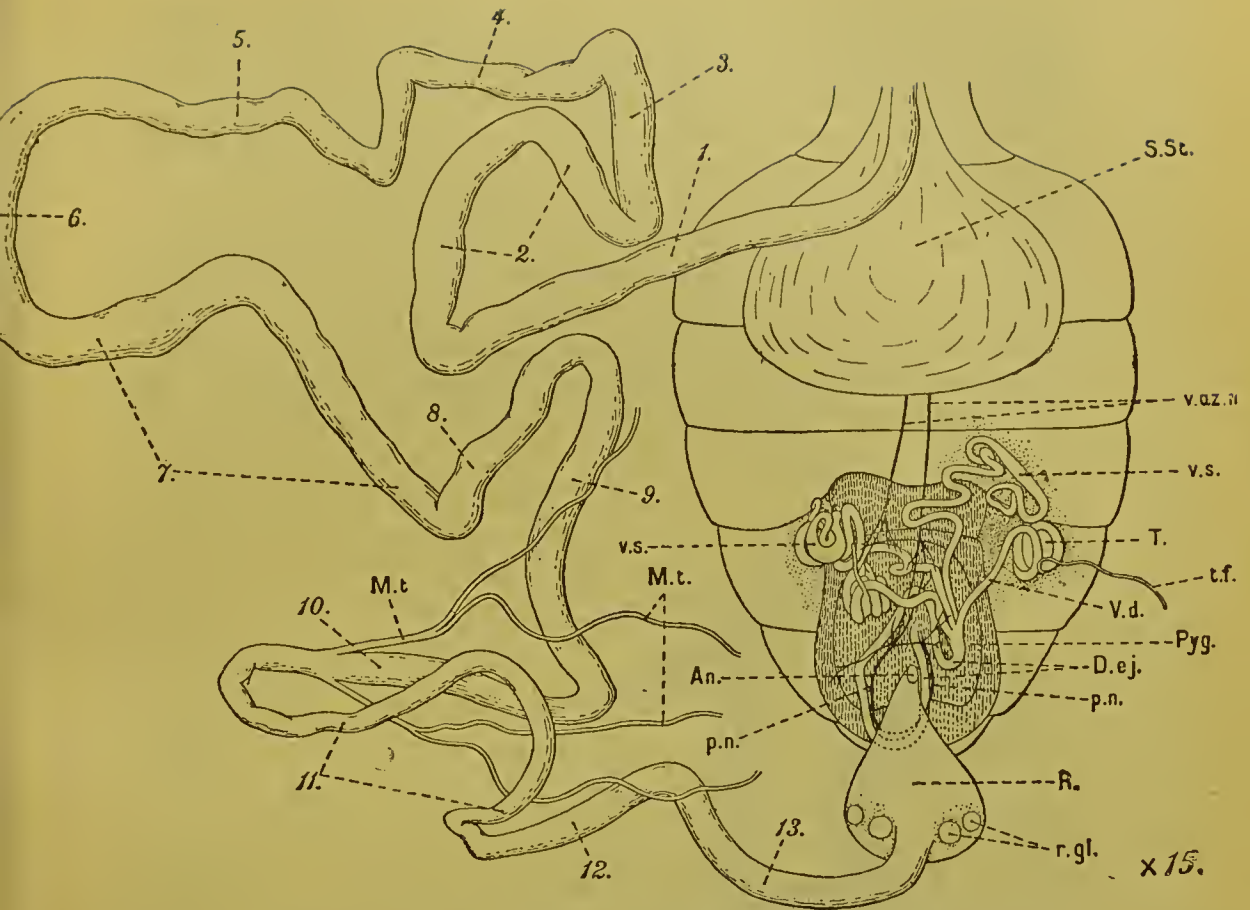


FIG. 5.—Dissection of the Abdomen, showing the Abdominal Intestine unraveled and turned over to the left side, and the Male Genitalia *in situ* in the Abdomen.

S. St., sucking stomach; 1—13, the limbs of the intestine, as indicated in the two previous figures; *M. t.*, *M. t.*, Malpighian tubules; *R.*, rectum; *r. gl.*, rectal glands; *An.*, anus; *T.*, testis; *t. f.*, testicular filament; *V. d.*, vas deferens; *v. s.*, *v. s.*, vesiculæ seminales, that on the left in its natural coil, that on the right unraveled; *D. e. j.*, ductus ejaculatorius; *Pyg.*, hypopygium; *v. az. n.*, branches of the ventral azygos nerve (genital nerve); *p. n.*, nerve to penis, following the ductus ejaculatorius.

The ductus ejaculatorius (*D. ej.*) has at its commencement a slight dilatation, into which open the four tubes just described. From this point the ductus runs a very short way backwards, then curves sharply forwards, but soon turns back again, passes across to the left side of the body, and forms a loop round the rectum, coming forward on the right to pass into the penis.

The various parts of the male generative organs are innervated, as already described, by a nerve plexus formed from the azygos abdominal nerve. There appears to be a small ganglionic swelling on the ductus ejaculatorius, whence arises a nerve (*p. n.*) which follows the ductus in its course to the penis.

The external organs of generation are concealed beneath the hypopygium. The penis is an organ of complicated structure and mechanism, with an armature of hooks, spines, hairs, and

semaphore-like erectile flaps, which would require so many figures to make their arrangement and relations clear, that I refrain at present from attempting any description of them.

The female genital organs differ considerably in appearance according as they are in the gravid or non-gravid condition. In the course of my dissections I have only found one female in the latter state. In the later periods of gestation the condition of the female is obvious externally, but females which do not appear to be gravid are found on dissection to have a small larva in the uterus.

The female organs (fig. 6) consist, like the male, of paired and unpaired portions. The former comprise the ovaries, the receptacula seminis and their ducts, and the uterine glands; the

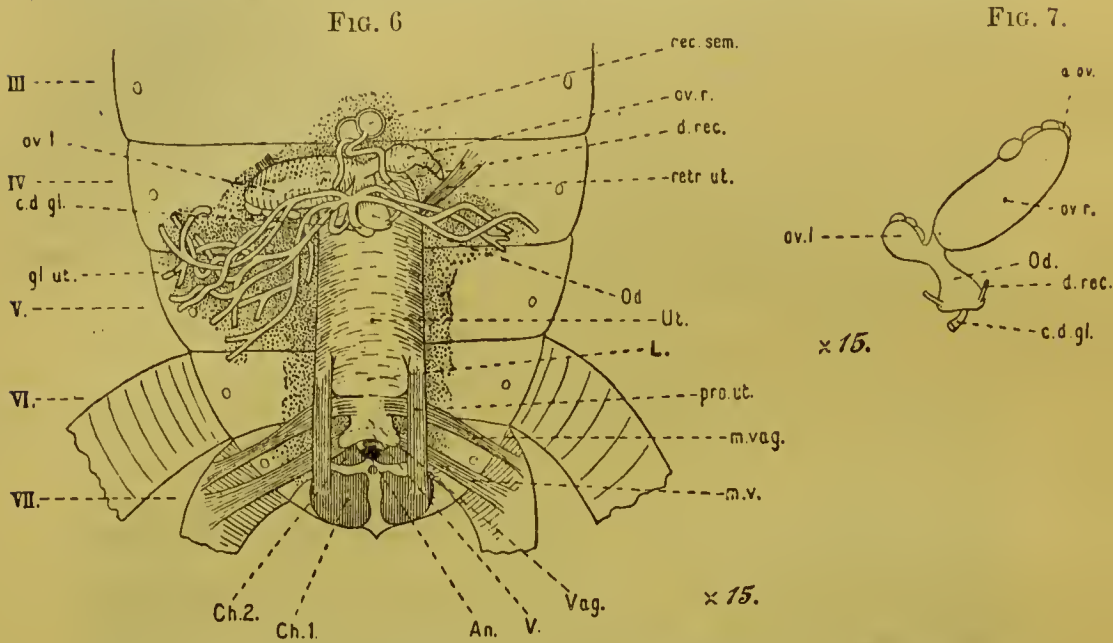


FIG. 6.—The Hinder Segments of the Abdomen with the Female Genital Organs *in situ*, dorsal view.

rec. sem., receptacula seminis; *ov. r.*, *ov. l.*, right and left ovarioles; *d. rec.*, duct of the right receptaculum seminis; *gl. ut.*, uterine glands (the greater number of these have been removed); *c. d. gl.*, their common duct; *retr. ut.*, retractor muscle of the uterus; *Od.*, oviduct; *Ut.*, uterus; *L.*, hinder extremity of the larva, causing a bulge in the uterus; *pro. ut.*, protractor uteri, attached to the chitinous plate (*Ch. 1*); *m. vag.*, muscle (dilator vaginae?) passing from the vagina to the tergum of the seventh abdominal segment; *m. v.*, muscle passing from the paired chitinous plate (*Ch. 2*) on each side of the vulva to the seventh tergum; *Vag.*, vagina; *V.*, vulva, the anterior margin of which is shown by a dotted line; *An.*, anus; *Ch. 1*, *Ch. 2*, paired chitinous plates.

FIG. 7.—The Ovarioles and Oviduct of a Non-gravid Female.

a. ov., apex of right ovariole; other letters as in the preceding figure. The very large ovum in the right ovariole has pushed the oviduct over towards the left side of the body.

latter are the oviduct, uterus, and vagina. The female system of organs is considerably modified from the condition usually found in insects, in relation to the fly's peculiar method of reproduction.

The ovaries are reduced to a single pair of ovarian tubes or ovarioles, one on each side of the body (figs. 6 and 7, *ov. r.*, *ov. l.*). Each ovariole shows only a small number of egg-chambers, not more than four or five. The lowest chamber is very much larger than any of the others, and contains a large ovum. When this ovum is comparatively small, the other egg-chambers are in a line with it (fig. 6, *ov. r.*), but as the ovum grows larger it grows past the other egg-chambers, so that they appear attached to the side of the ovum (fig. 6, *ov. l.*, fig. 7, *ov. l.*, *ov. r.*).

The two ovarioles are always asymmetrical, owing to the fact that the ova in the lowest egg-chambers reach full growth on each side alternately, so that if there is a large ovum on the left, there will be a smaller one on the right, and *vice versa*. The largest ovum I have seen was from a non-gravid female (fig. 7, *ov. r.*), and was probably nearly, if not quite, full-sized.

The two ovarioles open into the short, broad oviduct (figs. 6 and 7, *od.*), which widens out at its lower end to open into the uterus slightly behind the proximal end of the latter.

At its distal expanded end the oviduct receives right and left the two ducts (*d. rec.*) of the receptacula seminis. The latter (*rec. sem.*) are small spherical bodies of a bright orange-yellow colour, surrounded by a whitish, transparent envelope. Examination of the receptacula stained and mounted in Canada balsam shows that the clear envelope is an epithelium of large cells, surrounding a thick chitinous membrane which gives these organs their peculiar colour, and which is too opaque for the contents to be seen except in sections, by which method the receptacula are seen to be filled with spermatozoa. The two receptacula are firmly attached to one another. From each comes off the slender white duct, slightly convoluted. The ducts are perfectly distinct from one another, and open, as described above, into the lower end of the oviduct.

Immediately below the opening of the oviduct into the uterus, a small tube debouches into the latter by a median dorsal aperture. This is the common duct of the uterine glands (figs. 6 and 7, *c. d. gl.*). After a short course it branches right and left into tubes, which branch again repeatedly, forming a great number of glandular tubes, which differ markedly in the gravid and the non-gravid condition. In the latter state the gland-tubes are relatively few and very slender. In the gravid condition, on the other hand, the tubes are very numerous, forming a tightly packed mass filling up the posterior end of the abdomen, and requiring to be pulled away to show the other parts of the generative system; further, the individual tubes are much thicker, and when stained and mounted, they take up the stain very deeply and appear very opaque. There can be no doubt that these glands serve for the nourishment of the larva in the uterus.

The uterus (*Ut.*) is a large thimble-shaped organ attached to the body-wall by a number of muscles. Two retractors (*retr. ut.*)

run forwards from the proximal end. There are two pairs of protractors, one dorsal, the other ventral; the former (*pro. ut.*) start from the sides of the uterus and pass backwards to a pair of chitinous plates (*Ch. 1*) at the posterior end of the body. The wall of the uterus is beset by a very large number of small tracheal tubes (not shown in the figure), and is thick in the non-gravid condition, but becomes thinner when stretched by the growth of the contained larva. In all gravid uteri that I have seen, the two papillæ at the hinder end of the larva cause a bulge in the lower end of the uterus (fig. 6, *L.*). When the larva reaches a certain size, the rings of its segments become plainly visible through the wall of the uterus; they could not be seen in the uterus drawn in fig. 6, but in another, slightly larger, they could be seen distinctly.

The vagina (fig. 6, *Vag.*) is a broad tube, considerably longer in the non-gravid than in the gravid condition, with a pair of dilator muscles (*m. vag.*) which are attached right and left just below its junction with the uterus, and pass outwards to be attached to the anterior margin of the tergum of the seventh abdominal segment. The vagina widens out slightly as it approaches the vulva (*V.*), which is a crescentic, transversely elongated aperture, separated from the anus by a small chitinous plate (*Ch. 2*), one of a pair from which two muscles (*m. v.*) arise and pass outwards to be attached to the seventh tergum, a little way behind the attachment of the vaginal muscles already mentioned. These muscles probably act as dilators of the vaginal aperture, and the five pairs of muscles described in the preceding lines are to be regarded as constituting the mechanism of parturition.

4. *The Vascular System* consists of the heart, in the abdomen, and its continuation, the thoracic aorta, in the thorax.

The heart occupies the five anterior segments of the abdomen, and is situated dorsally immediately below the plates of the terga. It is so imbedded in the fat-body and pericardial tissue that not much can be made out of its structure by dissection alone, and examination of it mounted as a preparation for the microscope is necessary. It can then be seen to have five chambers, each with a pair of ostia and a pair of alary muscles, corresponding to the segments in which it lies. The alary muscles pass out at right angles to the axis of the heart, and can be traced through the fat-body to their attachments at the external lateral margins of the tergal plates.

The hindermost chamber of the heart appears to end blindly posteriorly. A little way in front of the hinder end are attached the two large alary muscles, the largest of the whole series; not far in front of these again are the two ostia, on the sides of the widest part of the chamber. In front of the ostia the lumen of the heart narrows rapidly, and to the narrowed portion is attached the next pair of alary muscles, lying in the hinder part of

segment IV. This arrangement is continued in segments II., III., and IV., the dilated portion of the chamber, with the ostia, occupying the middle of the segment, while the alary muscles, attached to the constrictions between the chambers, lie in the posterior regions of the segments. The alary muscles of these three segments are of moderate size. In segment II. the heart receives a pair of tracheal tubes, right and left, which come to it opposite the ostia, and fork at once into branches running forwards and backwards. The alary muscles corresponding to the first abdominal segment are very small and difficult to make out, and the region of the heart to which they are attached does not show the slightest diminution or constriction of its lumen, as is the case in all the chambers posterior to it. In front of the first pair of alary muscles, at the usual interval, are the two ostia, quite similar to those of the other chambers. In front of the first pair of ostia the lumen of the heart narrows to form a thin-walled vessel, which passes through the waist to become the artery which I have termed above the thoracic aorta. This last runs along the thoracic intestine on its dorsal side, and is continued over the proventriculus, remaining apparently quite independent of the digestive tract, and only loosely attached to it, until it reaches the œsophagus. Here it is firmly attached and becomes considerably dilated. A short distance in front of the proventriculus a conspicuous cushion-like mass of large cells lies over the aorta. At first I took this structure for a ganglion, but it appears to be a sort of lymphatic gland, judging from its appearance in sections. The thoracic aorta is apparently continued through the neck into the head, but I have not been able to follow its course further than the thorax.

The microscopic examination of the heart shows further that its floor is composed chiefly of fusiform cells resembling unstriped muscle-fibres, while its sides are made up of gigantic cells with nuclei of corresponding proportions. These cells are arranged with perfect regularity, and in a manner exactly similar on the two sides of the heart. Each ostium is formed by two cells, which are of small size when compared with the huge cells building up the wall of the heart, but are very large when compared with the cells of the surrounding tissues. Two of the giant cells intervene on each side between the hinder end of the heart and the fifth pair of alary muscles; two more between these muscles and the ostia next in front of them; and so on with unfailing regularity all the length of the heart, each ostium being separated from the alary muscles next in front or behind by just two giant cells. In front of the first pair of ostia are found two cells of the usual size on each side, then a pair of slightly smaller cells, which pass on into the walls of the thoracic aorta. Thus, not counting the ten couples of smaller cells which compose the five pairs of ostia, the entire wall of the heart is built up of 23 pairs of giant cells; to wit, four pairs to each of the five chambers, two additional pairs behind the fifth pair of alary muscles, and one pair anteriorly, making the transition to the thoracic aorta.

- . In view of the fact that the thoracic vessel is itself to be considered as a modified anterior portion of the heart, it is interesting to find that its delicate wall contains very large, flattened nuclei, arranged in pairs, right and left.

The alary muscles consist of delicate fibrils, arranged in an irregular fan-like manner, uniting into a stout muscle-fibre which is distinctly striated.

21. *GLOSSINA PALPALIS* IN ITS RELATION
TO *TRYPANOSOMA GAMBIENSE* AND
OTHER TRYPANOSOMES (*Preliminary Report*).

By E. A. MINCHIN, M.A., Professor of Protozoology in the
University of London, Lieut. A. C. H. GRAY, R.A.M.C.,
and the late Lieut. F. M. G. TULLOCH, R.A.M.C.
(Sleeping Sickness Commission).

[*Reprinted from* PROCEEDINGS OF THE ROYAL SOCIETY,
Series B, Vol. 78.]

[PLATES 1-3.]

In this paper we propose to give a brief statement of the results obtained by us with reference to the relation of the tsetse-fly (*Glossina palpalis*) to the trypanosome of sleeping sickness (*Trypanosoma gambiense*), and to other species of trypanosomes which this fly carries.

Our investigations have consisted of observations and experiments upon (A) Flies fed in the laboratory on animals which had been infected by the inoculation of cerebro-spinal fluid from sleeping sickness patients, and which showed trypanosomes in their blood as the result of such inoculation. (B) Flies caught in various localities which were found on dissection to contain trypanosomes in their digestive tracts.

Of the trypanosomes under the latter heading (B) we have found two distinct types. One of these types has been named by Professor F. G. Novy* *Trypanosoma grayi*, and one of us (Professor E. A. Minchin) proposes to call the other type *Trypanosoma tullochii*.

Type I. *T. tullochii*, n. sp. Minchin.—This type is distinguished by its more rounded nucleus placed near the middle of its body, by a small, usually circular, blepharoplast placed well behind† the nucleus, *i.e.*, at the end furthest from the flagellum (Plate 3, figs. 53-60).

* "Journal of Infectious Diseases," vol. 3, No. 3 (May, 1906), pp. 394-411, Plates 15-17. Professor Novy gives some excellent microphotographs of these trypanosomes, taken from preparations sent him by Lieutenant Gray.

† In this memoir we use the terms anterior and posterior purely with reference to the direction of locomotion of the trypanosomes described by us, and without prejudice to the disputed morphological questions involved.

Type II. *T. grayi*, Novy.—This form is characterised by its large nucleus, which may be oval, spherical, or compressed, and which is in all cases situated not far from the posterior end of the body. In many cases the nucleus shows distinctly eight chromosomes. The blepharoplast is large, transversely elongated, and situated close to the nucleus, either at its side or more usually anterior to it. Sometimes, however, it may be posterior to the nucleus, a point which we discuss further below. The flagellum is often distinctly thickened at the tip. This type varies very greatly both in form and size. We distinguish (1) male forms, very slender, with long free flagellum, with nucleus very compressed, and with the blepharoplast situated in front of it (Plate 2, figs. 21 and 22). Some of the forms reach an extraordinary length (Plate 2, fig. 33). (2) Female forms which are bulky, often thickened at the posterior end and with an oval or rounded nucleus. The blepharoplast is variable in position, and the free flagellum is very short (Plate 2, figs. 23–25 and 34). (3) Young forms (Plate 2, figs. 31 and 32) and indifferent forms, varying greatly in character; among the latter we may particularly note forms which are nearly spherical (Plate 3, figs. 43–51). The very protean character of these forms (*see* Plate 2, figs. 35–40; Plate 3, figs. 41–52) make it very uncertain as to whether they are really all of the same species. Since, however, we have noticed a marked difference between trypanosomes from flies which had fed after being caught and those in flies that had not fed (Plate 2, figs. 33 and 34, and Plate 3, fig. 41), we think that these variations of type are to be explained as the result of the conditions of nutrition of the host. The forms from flies which had not been fed were both scarcer and larger than those from flies which had recently sucked blood. In flies dissected soon after feeding it was found that small forms (Plate 2, figs. 31 and 32) largely predominated, and dividing forms were numerous (Plate 2, figs. 27, 28, and 29); on the other hand, in those cases in which flies were found to contain forms of a more indifferent character (Plate 2, figs. 36–40), it was noticed that stages of division were extremely rare, and that aggregations of similar forms into large masses were frequent (Plate 3, fig. 42).

The mode of division in *T. grayi* is noteworthy and characteristic. The two sister individuals which result from it are markedly unequal in size and differ also in the relations of their nucleus and blepharoplast. The smaller of the two has the blepharoplast placed in what may be considered the normal position, that is to say, well in front of the nucleus. On the other hand, the larger individual has the blepharoplast placed behind the nucleus (Plate 2, fig. 28). We consider, therefore, that the forms not infrequently found, in which the blepharoplast is situated behind the nucleus, represent, in many cases at least, the larger of two sister individuals resulting from recent division. Multiplication by division has only been observed by us in

individuals of indifferent or female type, never in fully differentiated male forms. Finally, we may draw attention to the numerous chromidia always present in young, indifferent, or female forms. In their staining reactions the chromidia seem to resemble the blepharoplast more than the nucleus.

(A) *Observations and Experiments with Flies Artificially Infected with T. gambiense.*—We undertook very numerous experiments to determine the exact mode of infection by the fly, particularly with the object of determining whether the fly became infectious at any definite period after having been fed on an infected animal. For instance, a batch of freshly caught flies was fed first on an infected animal, and then fed on successive days on a series of healthy animals, using a fresh animal for each feed; the experiments covering a period of 22 days from the time of the original infection of the flies. All such experiments, however, gave entirely negative results. On the other hand we obtained positive proof that *G. palpalis* can convey trypanosomes by means of its proboscis from an infected to a healthy animal, if it goes straight from one to the other. Our method of experimenting was as follows: A single fly was placed in a test-tube and the mouth of the tube covered with gauze. The mouth of the tube was then pressed on to the infected animal and the fly carefully watched. When the fly had about half fed it was removed from the infected animal and placed on a healthy one, on which it was allowed to finish its meal. Infection by trypanosomes was effected by this means in four out of five experiments when *G. palpalis* was used as the transmitting agent, and once out of four experiments when a *Stomoxys* was used in a similar manner. In order to determine further whether in these cases the infection was brought about by contamination with the fly's proboscis only or by the possible regurgitation of already ingested trypanosomes from the digestive tract, a further series of experiments was carried out, in which the fly, after having partially fed on an infected animal, was then allowed to feed on two healthy animals in succession. Five such experiments were carried out, in each of which it was observed that the fly (*Glossina*) had sucked blood from both the infected and the two healthy animals. In every case the *first* of the two healthy animals, and only the first, was infected, even when the fly had only been allowed to dip its proboscis for a moment into the first healthy animal and was then immediately transferred to the second healthy animal. This shows, in our opinion, that the infection is conveyed by contamination of the proboscis, and that if the fly be allowed to clean its proboscis by piercing the skin of one animal, it is no longer infectious to a second. In these experiments upon direct transmission the "Jinja" cattle-trypanosome was used by us, because it is abundant in the blood of infected animals (rats) with which we were working, and also on account of the fact that the infection or non-infection of a rat with this trypanosome is a matter of

certainty within a very few days, whereas had we used *T. gambiense* the results of our experiments would have remained uncertain for a very long while.

It has also been proved by the experiments of Bruce and by ourselves that freshly caught specimens of *G. palpalis*, at Entebbe, are capable of infecting animals with the trypanosome of sleeping sickness, but in this case all experiments seem to show that the number of fly-bites required to produce infection is a very variable one indeed, since over and over again more than 1,000 flies have fed on a susceptible animal without infecting it. The smallest batch with which we ourselves have been successful in producing infection consisted of 134 flies.

Observations on the fate of trypanosomes, introduced into the digestive tract of the tsetse-fly by feeding it in the laboratory upon animals infected with *T. gambiense* gave the following results:—The trypanosomes, never very numerous in the ingested blood, show at the end of 24 hours a slight increase in number, and many of the parasites are observed in stages of division. At the same time they have become differentiated into two very distinct forms. The first is a very slender type with cytoplasm free from granules, with the nucleus sometimes rounded but more usually compressed, and with a considerable length of free flagellum (Plate 1, figs. 1 to 6). Many of these slender forms are observed at this stage to be in the act of extruding granules of chromatin from the nucleus (Plate 1, figs. 4 to 6). The second form of parasite is relatively very large and bulky with granular and deeply-staining cytoplasm, with very large spherical nucleus, with short free flagellum, and with the blepharoplast often some distance from the posterior end (Plate 1, figs. 7 to 14). These two forms may be regarded, on the analogy of developmental facts recorded of other trypanosomes, as male and female respectively. In both forms stages of division were observed, but in no case have we succeeded as yet in observing with certainty any process of conjugation. The two forms are easily distinguished in the living condition, the slender males being also characterised by much greater activity than the bulky females.

Male and female forms could also be recognised in the blood of the experimental animals (monkeys) especially in films fixed with osmic vapour. In films dried in the ordinary way, the characteristic differences were much less distinct. In either case the differentiation of sexual characters is far less marked than it becomes in the intestine of the fly. Trypanosomes of male character (Plate 1, fig. 16) are common in blood-films, but those of female character (Plate 1, fig. 17) are very scarce, and only two were found, both of which were remarkable for having the nucleus composed of four distinct masses of chromatin. On the other hand, an abundant form in the blood films is an indifferent type (Plate 1, figs. 18 and 19), characterised usually by very short free flagellum, and it is this form which develops into

the female form in the fly. In this connection attention should be drawn to the forms, distinctly of the female type, obtained by two of us (Gray and Tulloch) in a culture (Plate 1, fig. 20, see Appendix II).

It may be pointed out that the sexual forms of *T. gambiense* from the tsetse-fly are very similar to the forms of *T. brucei* described by Koch* from other species of Glossina, so far as can be judged from Koch's figures. It is our opinion, however, that many of the forms described by Koch as developmental stages of *T. brucei* are really stages of one or more distinct aspects of trypanosomes carried by the flies, comparable to, and perhaps identical with, *T. grayi* and *T. tullochii* in *G. palpalis*.

At 48 hours after feeding the trypanosomes are still numerous in the intestine of the fly, and a type of more indifferent character begins to make its appearance (Plate 1, fig. 15). At 72 hours the trypanosomes are usually beginning to become more scanty and difficult to find in the digestive tract of the fly, although in some cases they are still numerous and chiefly of the indifferent type. At 96 hours, in almost every case, not a single trypanosome could be found even after the most careful searching. In one case a single trypanosome was found, and in another case two, on the fourth day, but in all other cases the trypanosomes seemed to have vanished completely at this period, and could never be found at any subsequent time. It would appear as if they died out with the absorption of the blood with which they were ingested, and were unable to pass forward in the digestive tract into the blood taken up by the fly at any subsequent feeding. In this they contrast sharply with the trypanosomes described above, occurring in the fly under natural conditions.

The disappearance of *T. gambiense* from the digestive tract of the tsetse-fly could be interpreted in one of three ways: (1) the trypanosomes may actually die out and be digested; (2) the trypanosomes may pass from the digestive tract into other organs of the fly; (3) the trypanosomes may become, by rapid division, so minute as to escape detection, like the forms of *Spirochaeta ziemannii* described by Schaudinn, or like the invisible micro-organism of yellow fever. In order to test the second of these two possibilities, the internal organs of a number of artificially infected flies were carefully examined, but always with negative results, while the experimental results of Bruce and ourselves seem to disprove infectivity of the fly at any period after 48 hours, and, therefore, render improbable the third possibility suggested above. So far then as it is possible to draw conclusions from our observations, it would appear that *T. gambiense* does actually die out in the tsetse-fly after the third day. In all cases *T. gambiense* was found only in the mid-gut of the fly, and appeared never to pass either backwards into the proctodæum or forwards into the proventriculus, another point in which they contrast with the "fresh fly trypanosomes."

* "Deutsch. Med. Wochenschr.," 1905, No. 47.

(B) *Observations and Experiments upon Freshly-caught Tsetse-flies Found to Contain Trypanosomes.*—When freshly-caught tsetse-flies were examined by us in the laboratory, either after having been fed upon a healthy animal or not, a certain percentage of them were found to contain trypanosomes of one or rarely of both types referred to above as *T. grayi* and *T. tullochii*. In such cases the trypanosomes were usually present in enormous numbers, especially if the fly had been previously fed. These trypanosomes, when compared with *T. gambiense* artificially introduced into a fly's intestine, are distinguishable by their appearance and movements. They are far more active than the sluggish *gambiense*, especially the male forms, which often shoot across the field of the microscope with the greatest rapidity. When moving in this way the body of the parasite remains nearly stiff, while the forwardly directed flagellum vibrates with rapid serpentine movements. In a few cases they were found in masses in the proctodæum, but in most cases they occurred in the intestine, swarming and multiplying in the freshly ingested blood. Occasionally they were found passing along the thoracic intestine into the proventriculus. The parasites found in the proventriculus did not differ appreciably either in size or appearance from those found in the digestive tract. By the method suggested by Koch, of compressing the bulb of the proboscis, we succeeded in forcing trypanosomes out from the proboscis, but only in those flies in which the parasites were found in the proventriculus. Of the two types described above *T. grayi* was the most commonly found, being present in 1.47 per cent. of a total of 3,000 flies examined, while *T. tullochii* was found in 0.17 per cent. of flies, and both trypanosomes together in the same fly only three times. When trypanosomes were found in the fly's proventriculus, it was more usually *T. tullochii* which was present, while when trypanosomes were found only in the fly's intestine, it was more usually *T. grayi* that occurred, but no conclusions can be drawn from this until more flies have been examined.

The object of our experiments on these "fresh fly trypanosomes" was to determine whether one or both of the two types found were or were not developmental stages of *T. gambiense*. As it is now beyond all doubt that *G. palpalis* is the agent which conveys the trypanosome of sleeping sickness from an infected to a healthy individual, it would seem most probable at first sight that any trypanosomes found in the bodies of these tsetse-flies caught in a sleeping sickness area would be developmental stages of *T. gambiense*. We felt no doubt at the outset of our investigations that these fresh fly trypanosomes were to be identified with *T. gambiense*. Koch* evidently worked on the same assumption, since in his comparison of the supposed developmental stages of *T. brucei* and *T. gambiense* there can be no doubt that he has taken the form which has been called *T. grayi* for a developmental phase of *T. gambiense*. As we

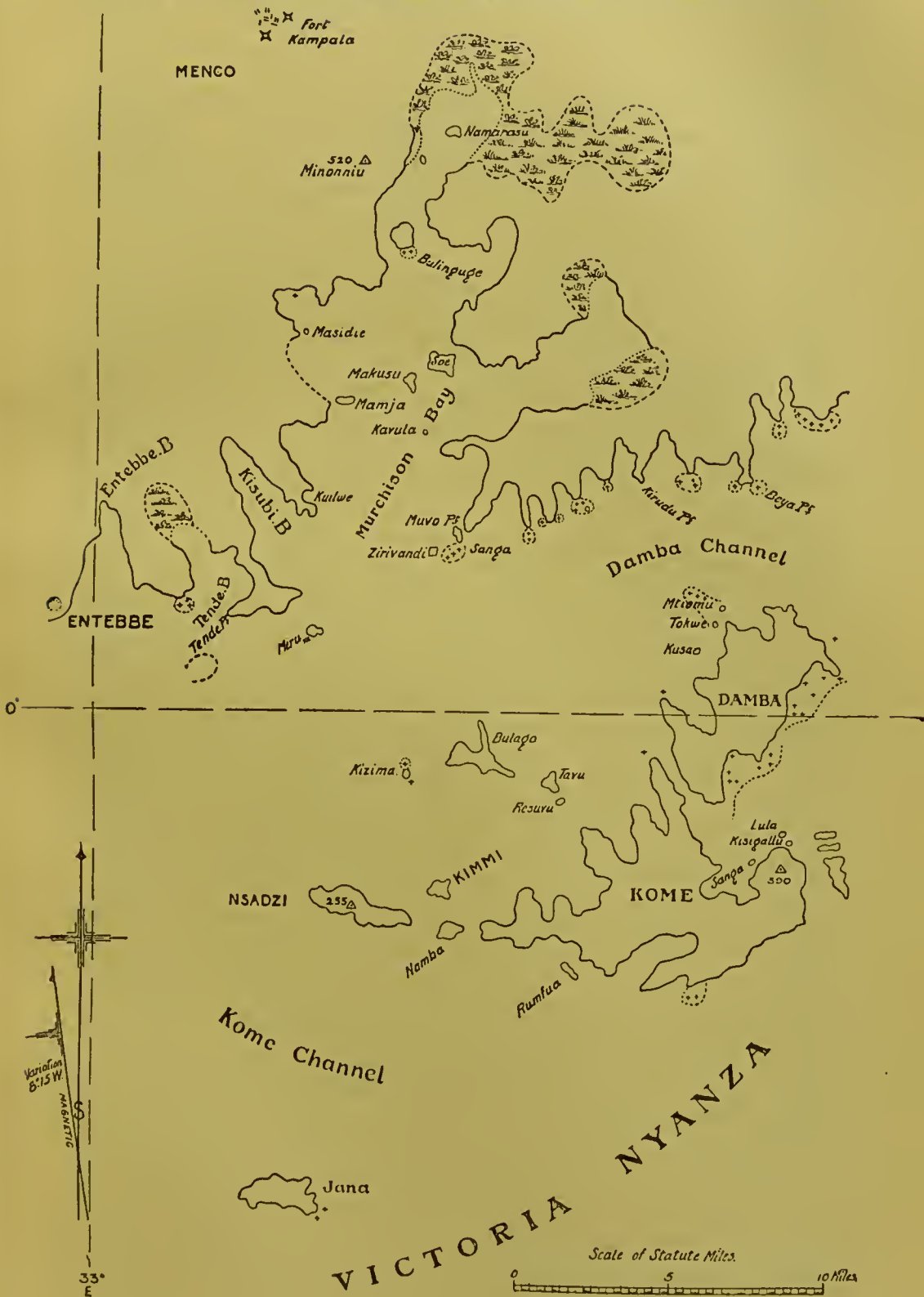
* "S. B. k. pr. Akad. Wiss. Berlin," 1905, pp. 958-262.

proceeded, however, with our investigations we were gradually led to doubt any connection between these "fresh fly trypanosomes" and sleeping sickness. In order to determine this point we carried out a number of experiments on flies caught on the island of Kimmi. This island was chosen because it swarmed with these tsetse-flies, of which a high percentage contained trypanosomes, and because it was, and has been for a very long while, quite uninhabited.

Kimmi is a small island of the Sesse group, about two miles long by a mile wide (*see* map). There is a narrow strip of sandy shore all round it, the remainder of the island being covered with thick undergrowth and forest. On the foreshore are many ambatch trees, where cormorants, other diving birds, and weaver birds are very plentiful. This island is a regular feeding ground for hippopotami and is crossed in all directions by their tracks. Crocodiles are also very numerous. Kimmi is situated about 15 miles from Entebbe and is two miles from Nsadzi Island in the one direction and from Kome Island in the other. For more than a year this island has been quite uninhabited and natives now never visit it. The whole island swarms with tsetse-fly (*G. palpalis*). In spite of the total absence of human beings on Kimmi Island, we found that more than 7 per cent. of the tsetse-flies caught there contained trypanosomes of one or other of the two types mentioned, while only 1.7 per cent. of the flies caught on the main land near Entebbe, a place with a numerous population, among whom sleeping sickness is common, contained similar parasites.

Our method of experimenting with these flies was as follows:—Our camp with our apparatus and experimental animals, was placed on the neighbouring healthy Island of Nsadzi, in a region free from fly and where there is no sleeping sickness. A steam-launch was placed at our disposal by the authorities and by means of it batches of flies were brought back from Kimmi, so that we were not obliged to take possibly infected native canoemen, a class among whom sleeping sickness is very common, to this island. These Kimmi flies were divided into batches and each batch assigned to a particular animal (monkey, rat, guinea-pig, or hen) on which the batch was fed at once, and again repeatedly on successive days. After 12 days or a fortnight of such daily feeding, the flies of each batch were dissected and examined for the trypanosomes which they might contain. In practically every case one or more flies of each batch were found to contain trypanosomes, so that every experimental animal was definitely known to have been fed upon repeatedly by at least one fly containing trypanosomes. Had these trypanosomes therefore been identical with *T. gambiense*, it might have been expected that at least some of these susceptible animals (such as monkeys, guinea-pigs, and rats) would have become infected, *but this did not occur in a single instance*. We thought that *T. grayi* might possibly be a bird-trypanosome, but the negative results of feeding flies containing it on fowls did not bear out this supposition.

PART OF THE SESSE ISLANDS



In addition to these feeding experiments, we inoculated other experimental animals of the same kinds with the contents of the various parts of the digestive tracts of flies containing these trypanosomes, some from the proventriculus, some from the intestine and some from the proctodæum, *but again in every case the results were negative.*

We are, therefore, now convinced from the results of these numerous experiments, of which a list is given on p. , *that the trypanosomes found in the freshly-caught tsetse-flies, and referred to by us as T. grayi and T. tullochii, have nothing to do with sleeping sickness and are not developmental stages of T. gambiense.*

It is a matter of regret to us that we have not been able to establish on what vertebrate host, if any, these trypanosomes are parasitic. It seemed at least probable that *T. grayi*, some forms of which greatly resemble *T. johnstonii*, Dutton and Todd* from *Estrelda estrelda*, was taken up by the fly from some of the numerous water birds that haunt the lake-shore. On the other hand, *T. tullochii*, which is very similar in its morphological characters to *T. gambiense*, might similarly be derived from a mammalian host. We may draw attention in this connection to the remarkable manner in which this tsetse-fly haunts the lake-shore. There is nothing in the breeding habits of the fly which should oblige it to frequent the vicinity of water, as in the case of the mosquito. Our experience of flies kept in the laboratory convinced us that a certain amount of moisture is necessary for them, since they died much faster in their cages if not kept over water. It may be supposed, however, that one attraction that the lake-shore exerts upon this voracious blood-sucker, is that of food-supply. Along the shores of the lake and on all the small islands are vast numbers of cormorants and other fish-eating birds perched with their wings extended, drying themselves in the sun on the trees, and especially on the ambatch-trees, where the flies are found in swarms. These birds might furnish one constant and important source of food. We found in the laboratory that tsetse-flies fed very rapidly on captive fowls, creeping under their wings to bite the poorly protected parts of the skin. On the other hand, when a heap of recently shot water-birds, some of which were hardly dead, were lying on the lake-shore at Kimmi Island, the swarms of tsetse-flies did not attempt to settle on them, although freely biting us and our servants. A second possible source of food supply is furnished by the aquatic animals of the lake shore, such as the hippopotamus, the otter, the crocodile and the python. We have definite evidence that the fly feeds on the hippopotamus and on the crocodile. Flies were caught in the act of biting a hippopotamus just recently shot, settling chiefly on the ears and nose. We, therefore, made blood-films and had blood-films sent us of as many aquatic birds and animals as possible, including five or six hippopotami. Only in a single case did we find a trypanosome, namely, in a not very

* Liverpool School of Tropical Medicine, *Mem.* XI. Pl. 2, fig. 1.

well preserved film of crocodile's blood ; beyond its large size and general resemblance to other reptilian trypanosomes, it was not

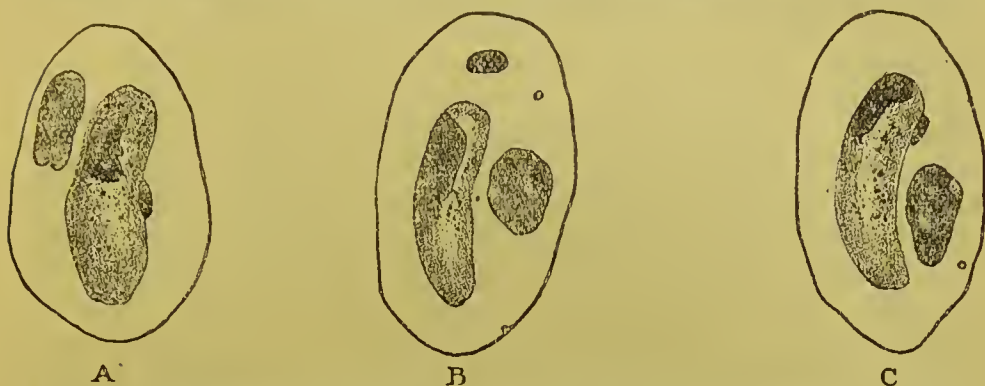


FIG. 1.—Hæmogregarine in the red blood-corpuscles of the crocodile. $\times 2000$.

possible to make out any details of structure in this parasite. We may mention, however, that the blood of many of the birds contained Halteridia, and that a Hæmogregarine was quite common in the blood of the crocodiles (fig. 1). We also observed that flies in captivity sucked the blood of lizards, chameleons and snakes very freely.

There are, therefore, two possible sources for the trypanosomes in the freshly-caught tsetse-flies. Either they are taken up from some of the numerous animals upon which the fly feeds, or they may be parasites of the fly itself, like *Herpetomonas muscæ-domestice* in the house-fly. In this respect it is interesting to note that a small percentage of another common blood-sucking fly in Uganda (*Stomoxys* sp.) contain a species of *Herpetomonas* very similar to that of the common house-fly in Europe. With regard to *G. palpalis* we were never able to obtain any definite proof that it fed on anything but blood. It is therefore difficult to understand how a parasite of the tsetse-fly itself could be conveyed from one fly to another except by the hereditary method. We have a single instance to record which certainly suggests hereditary transmission of these trypanosomes. A tsetse-fly was bred in the laboratory in August and was fed for two months on fowls, which were unfortunately also used for feeding our stock of tsetse-flies in our breeding cages. On October 9, the fly was fed on a monkey showing very scanty trypanosomes (*T. gambiense*) in its blood. The next day 21 hours later, this fly was dissected and found to contain a few scanty *T. gambiense*, one of which is figured on Plate 1, fig. 14, and vast swarms of *T. grayi* (Plate 2, figs. 23 and 28). It is obvious, therefore, that this fly was either infected with *T. grayi* when it emerged from its pupa or that it became infected from one of the fowls which had possibly been infected in its turn by the fresh flies which fed on it. It may be mentioned in this connection that experiments directed towards obtaining flies infected with *T. gambiense* by the hereditary method, that is to say, by breeding from flies fed continually on infected animals, gave no result.

In conclusion, one remarkable experiment of ours may be mentioned. At our camp on Nsadzi, referred to above, we fed a large number of freshly-caught Kimmi flies on a goat which we obtained from natives on the island. We then dissected these flies and, to our astonishment, could not find trypanosomes in a single one of some 500 flies which had so fed, whereas in other Kimmi flies, caught at the same time, which had fed on our other experimental animals (monkeys, etc.), trypanosomes were present in the usual proportion. We then prepared some goat's serum and added a drop of it to the contents of a fly's intestine teased out on a slide, which contained *T. grayi* in large numbers. Another drop of this same goat's serum was added to a preparation of *T. gambiense* obtained from an infected rat and the two preparations watched. It was found that in the preparation of *T. grayi*, the trypanosomes rapidly became immobile and died off, while the *T. gambiense* remained active. We then tried the same two experiments over again, using human serum instead of the goat's serum, and then found that the trypanosomes were not affected in either case. This result seems to us to furnish an additional means of distinguishing between *T. gambiense* and *T. grayi*.

APPENDIX I.

Table I.—List of Animals on which Tsetse-flies known to contain Trypanosomes of the two types mentioned have fed. All these animals remained uninfected by this feeding.

Animal.	Number of flies which had fed found to contain trypanosomes.	Class of trypanosome present in fly.	Presence or absence of trypanosomes from fly's proventriculus.
Monkey No. 370 ...	2	<i>T. grayi</i> .	
" No. 391 ...	3	"	
" No. 369 ...	2	"	
" No. 397 ...	1	"	Present.
" No. 335 ...	3	<i>T. grayi</i> in two flies. <i>T. tullockii</i> in one fly.	Present in one of the former.
" No. 474 ...	2	<i>T. grayi</i> in one and <i>T. tullockii</i> in the other.	Present in both.
" No. 499 ...	4	<i>T. grayi</i> .	Absent in all.
" No. 525 ...	5	"	
" No. 553 ...	1	"	Absent."
" No. 554 ...	4	"	Present in one fly.
" No. 473 ...	2	<i>T. grayi</i> in one and <i>T. tullockii</i> in the other.	Present in both.
" No. 498 ...	4	<i>T. grayi</i> .	Absent in all.
" No. 555 ...	1	"	Absent.
" No. 556 ...	3	"	Present in two.
" No. 557 ...	1	<i>T. grayi</i> and <i>T. tullockii</i> together.	Present.
Guinea-pig, F. F. ...	8	<i>T. grayi</i> in 7. <i>T. tullockii</i> in 1.	Present in two.
" No. 528 ...	5	<i>T. grayi</i> .	Absent.
Rat (white), No. 533 ...	1	<i>T. tullockii</i> .	Present.
Hen No. 505 ...	4	<i>T. grayi</i> .	Present in two.
Hen No. 506 ...	6	<i>T. grayi</i> in 5. <i>T. tullockii</i> in 1.	Present in three.

APPENDIX II.—*An Experiment on the Cultivation of T. gambiense.*

By Lieutenant A. C. H. GRAY, R.A.M.C., and the late Lieutenant F. M. G. TULLOCH, R.A.M.C. (Sleeping Sickness Commission).

Our numerous failures in this direction have been attended by one partial success.

The following method was employed. A tube of agar, prepared according to the formula of McNeal and Novy, was melted and cooled to 60° C. Three times its volume of blood, taken directly from the heart of a dog without defibrination, was added to the agar. The water of condensation was inoculated with a drop of blood from a white rat (No. 513) very rich in trypanosomes. On examining the tube six days later a few living trypanosomes were found, which appeared similar to the forms inoculated. On the 8th and 10th days no trypanosomes were seen in a loopful of fluid withdrawn from the tube. On the 15th day several active trypanosomes were seen in a sample. These trypanosomes were found singly and in groups of three or four. Dividing forms were also seen. These forms were distinctly larger than the trypanosomes originally inoculated, and on measurement were found in some cases to be as long as 54 μ . Besides being longer and broader than the trypanosomes in the blood of the rat the position of the micro-nucleus was different (Plate 1, fig. 20). In the trypanosomes from the test-tube the micro-nucleus was situated at a considerable distance from the hinder end of the parasite and consequently nearer to the macro-nucleus. These trypanosomes closely resembled certain forms which we have found in the stomach and intestinal tract of tsetse-flies, 24 hours after being allowed to feed on infected monkeys. On the 17th day trypanosomes were still present in about the same numbers but a few cocci were also found in the tube. Up to the 20th day trypanosomes were still found, but were sluggish in their movements and became fewer in number as the cocci increased. After this date the growth of cocci became profuse and the trypanosomes died off. Up to the present (seven days) no trypanosomes have been found in sub-cultures made from this tube although the latter are free from bacteria.

As multiplication had commenced in the original tube it is reasonable to expect that a successful culture would soon have resulted if it had not become contaminated by cocci.

The resemblance of the newly-formed trypanosomes to forms seen in tsetse-flies after feeding on infected animals is of interest.

APPENDIX III.—*Some Notes on a Herpetomonas found in the Alimentary Tract of Stomoxys (calcitrans?) in Uganda.*

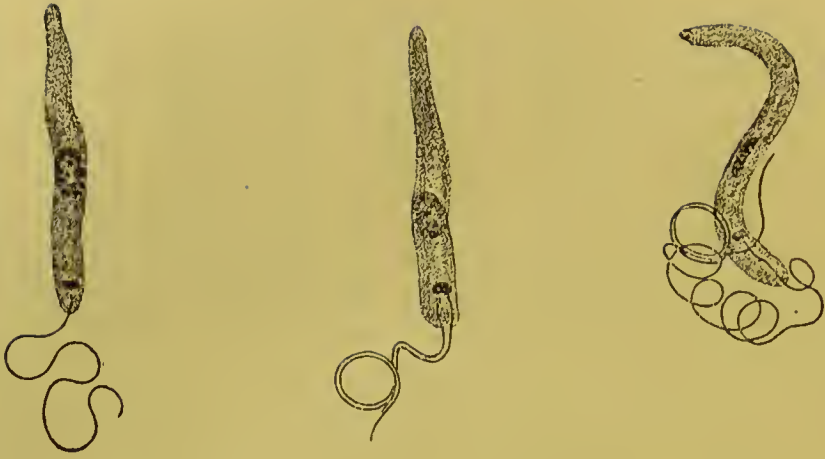
By Lieutenant A. C. H. GRAY, M.B., R.A.M.C.

In the course of examining the contents of the alimentary tract of some specimens of *Stomoxys (calcitrans?)*, which had previously been allowed to feed themselves on a monkey infected with the trypanosome of sleeping sickness, I found a species of *Herpetomonas* in the alimentary tract of three flies out of a total number of 280 examined.

In its movements, size, and general appearance, the flagellate seemed to closely resemble *H. muscæ-domesticæ* of the common house-fly.

In two flies, this parasite was present in very large numbers. Those two flies were full of blood from the monkey they had fed on 24 hours previously, and in this blood, practically unaltered *T. gambiense* were present in scanty numbers. In the third fly, this *Herpetomonas* was present in very scanty numbers and no trace of recently ingested blood could be found in it.

Films, fixed in osmic acid and stained with Borrel blue and eosin, showed that the commonest type of this parasite measures from 35 to 50 μ (figs. 1, 2, 3).



FIGS. 2-4.—*Herpetomonas* from the gut of *Stomoxys* (*calcitrans* ?); fig. 2, common form with single flagellum, and with nucleus broken up into separate masses; fig. 3, commonest form, with double flagellum; fig. 4, form with compressed nucleus and very long flagellum.

The body of the parasite is cylindrical, with a rounded anterior and more pointed posterior extremity. The protoplasm of the body stains rather deeply. A large rounded nucleus is placed at the centre of the body of the parasite. The chromatic substance of the nucleus is sometimes seen to be broken up into granules (chromosomes), apparently 14 in number, contrasting in this respect with *H. muscae-domesticae*, in the nucleus of which eight chromosomes are present (Prowazek). The blepharoplast is oval or kidney shaped, of a large size and stains deeply. It is placed close to the origin of the flagella and to the anterior rounded extremity of the body of the parasite. The double flagellum arises close to the blepharoplast and may reach an enormous length in some individuals (fig. 3).



FIGS. 5-7.—*Herpetomonas* from gut of *Stomoxys*; fig. 5, small form with dividing nucleus; fig. 6, small form showing the posterior position of the blepharoplast, and long intracellular course of the flagellum; fig. 7, small form, ordinary type.

Besides these large forms, smaller individuals are present (figs. 4, 5, 6). The bodies of these parasites stain more faintly than the above and are often curved. The nucleus is more compressed. The blepharoplast is smaller and situated at a greater distance from the anterior extremity of the body. The single flagellum arises close to the blepharoplast and consequently has a somewhat longer course through the body of the parasite. It emerges as a short, thick, free flagellum.

Both these forms commonly undergo longitudinal division. In some cases the nucleus apparently divides before the blepharoplast.



FIGS. 8-10.—*Herpetomonas* from gut of *Stomoxys*, non-flagellated forms; fig. 8, mass of blue-staining protoplasm containing one large chromatin body; figs. 9 and 10, masses of protoplasm containing paired chromatin bodies.

In the third fly non-flagellated forms were found to occur (figs. 7, 8). Masses of blue-staining protoplasm containing chromatin bodies in pairs (fig. 9) were also rarely found in this fly. Every such pair of chromatin bodies consisted of a larger and a smaller separate portion. The larger portion is circular and more faintly staining, the smaller is oval and more deeply staining. These paired masses of chromatin suggest a form analogous to Leishman-bodies.

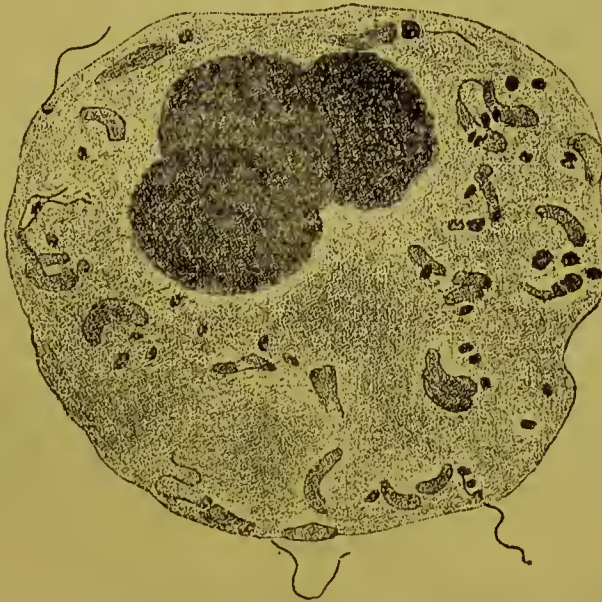


FIG. 11.—Large cell (probably a leucocyte) from contents of gut of *Stomoxys* (*calci-trans*?), containing in its interior large numbers of disintegrated *Herpetomonas* forms.

On several occasions, in the first two flies, large cells (leucocytes?) were found containing in their interior the broken-up remains of large numbers of the *Herpetomonas* (fig. 10).

The figures illustrating these notes are all $\times 2000$ and drawn with the camera lucida from slides fixed in osmic acid and stained with Borrel blue and eosin.

DESCRIPTION OF PLATES.

PLATE 1.

Trypanosoma gambiense, figs. 1-14, forms from the gut of the tsetse-fly (*Glossina palpalis*) one day after infection (i.e. about 24 hours) after being taken up by the fly. Fig. 15, two days (48 hours) in the fly. Figs. 16-19, forms from the blood of a monkey (*Cercopithecus* sp.) infected with the injection of cerebro-spinal fluid from a sleeping sickness patient. Fig. 20, culture form from blood of infected rat, 15th day. All except figs. 14 and 20 preserved wet with osmic vapour stain, Leishman or Giemsa. $\times 2000$.

Figs. 1 and 2, male form with compressed nucleus. Fig. 3, male form with rounded nucleus. Figs. 4 and 5, similar forms with chromatin being given off from the nucleus. Fig. 6, male form dividing chromatin being given off from both the daughter nuclei. Figs. 7-14, female forms, figs. 7 and 12 dividing. Fig. 15, indifferent form. Fig. 16, male form. Fig. 17, female form, very scarce (only one other was found). Figs. 18 and 19, indifferent forms which in the fly become female; note the short, free flagellum. Fig. 20, female form from culture tube, 15th day.

PLATE 2.

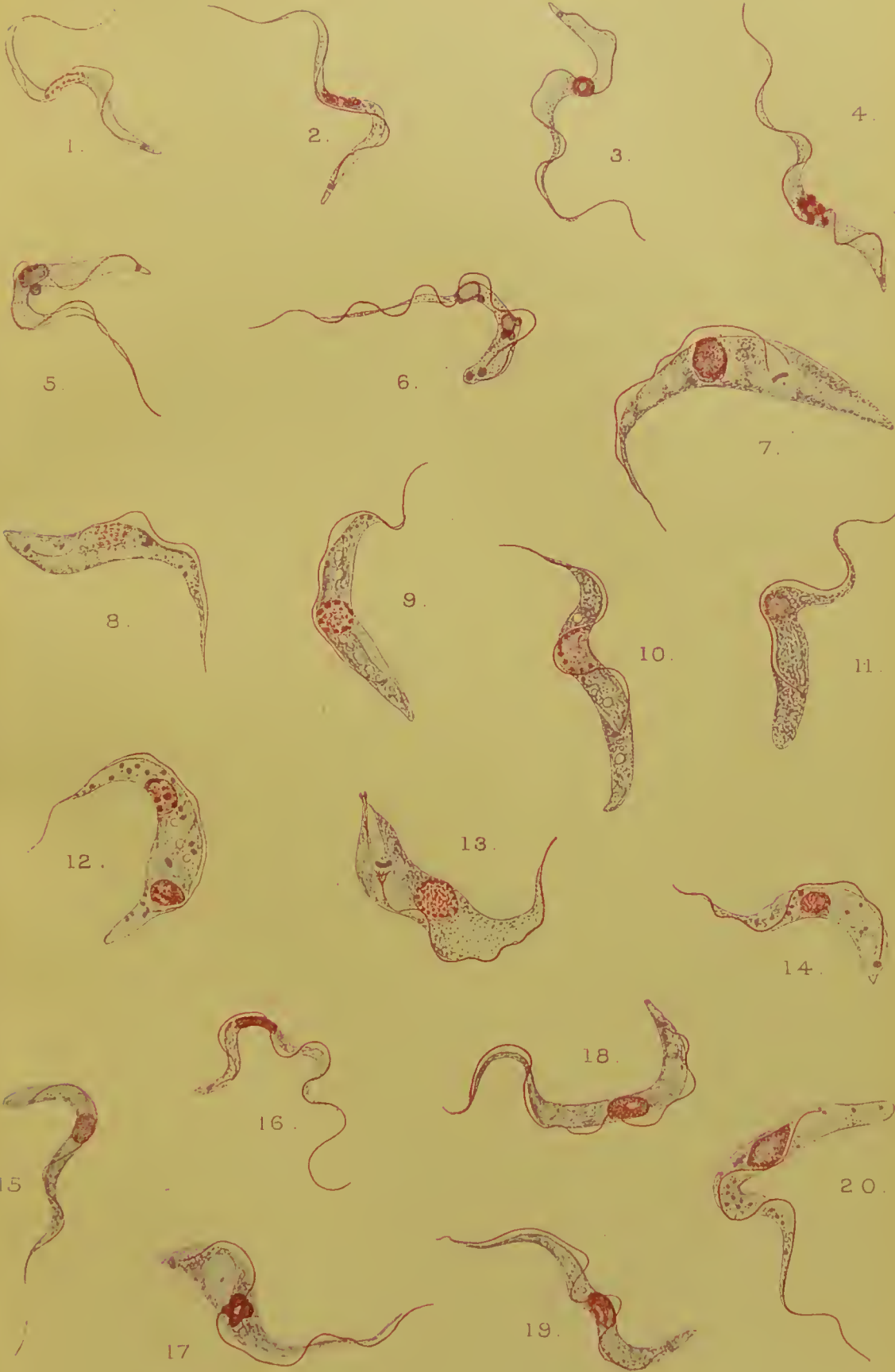
Trypanosoma grayi, figs. 21-30, from the gut of the tsetse-fly (*Glossina palpalis*). The flies from which these trypanosomes were obtained had been fed regularly on the blood of neutral monkeys and were dissected after about 10 days of such feeding. In all cases the whole gut of the fly swarmed with thousands of similar trypanosomes. Figs. 31 and 32, small forms; flies dissected 24 hours after their first feed of blood generally contained forms such as these in very great abundance, many dividing forms were also present, larger forms, as above, were rare. Figs. 33-35, trypaunosomes from fresh-caught tsetse flies, which had not fed on blood for a long while. In such flies, parasites were never very numerous, and the types present were all of a large size. Figs. 36-40, various other types from flies which had fed on blood. Fixed in alcohol, stained with Leishman or Giemsa. $\times 2000$.

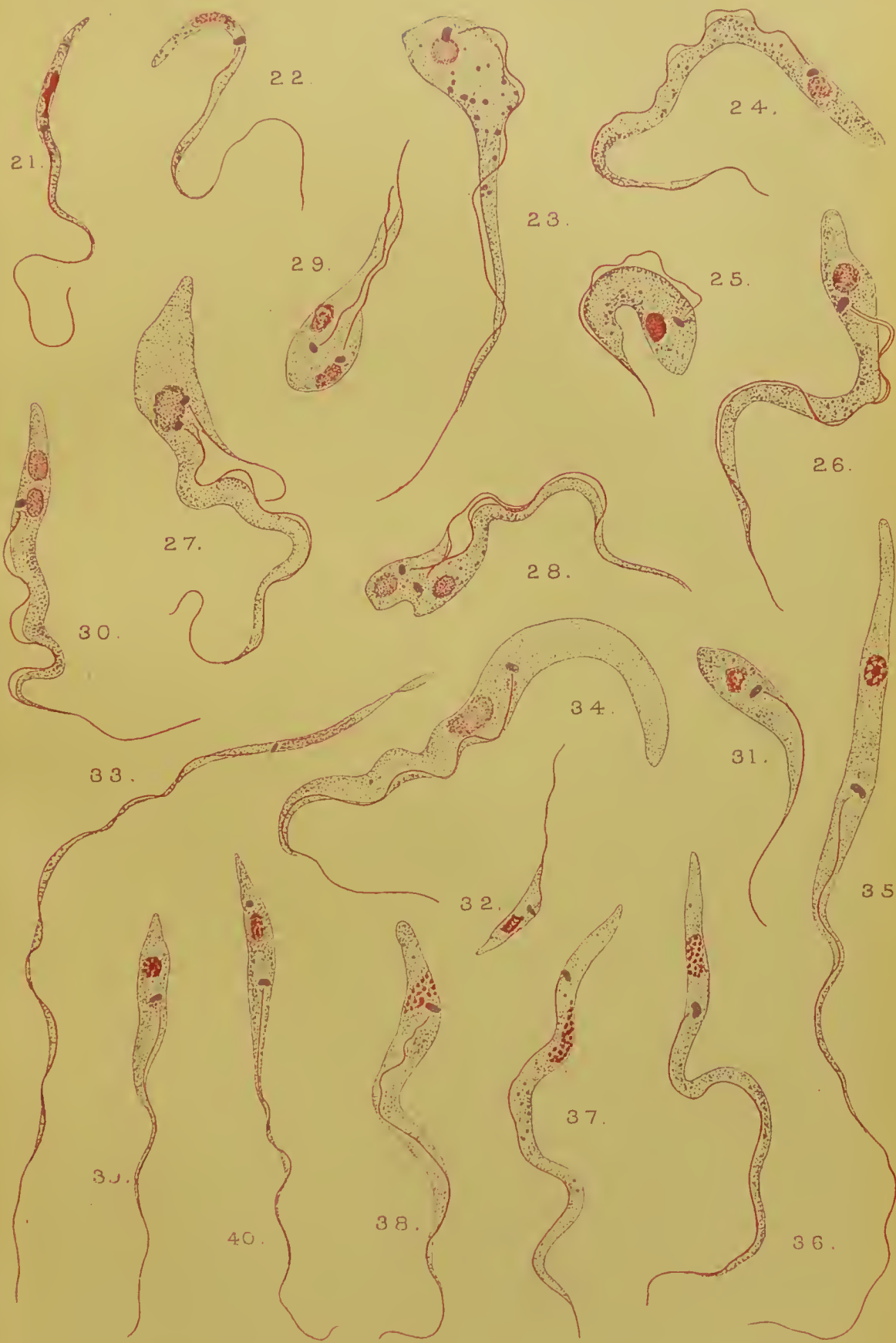
Figs. 21 and 22, male forms with compressed nucleus and long free flagellum. Figs. 23, 24 and 25, female forms. Posterior extremity thickened, short free flagellum. Figs. 26, 27 and 28, stages of division showing the unequal size of the two resulting individuals. Fig. 29, division of a small form into two more or less equal-sized individuals. Fig. 30, aberrant dividing form, in this case the nucleus has already divided, whereas the blepharoplast has not yet done so. Figs. 31 and 32, young forms resulting from the unequal division of a large female form. Fig. 33, very long male form. Fig. 34, very large female form. These two forms occur in flies which have not fed on blood for a long time. Fig. 35, very long form, with nucleus consisting of eight chromosomes. Figs. 36-40 are all from the same fly. Figs. 36, 37, and 38 show the nucleus broken up into separate chromatic granules, and the varying position of the blepharoplast. Fig. 39, young form showing regular division of the nucleus into eight chromosomes. Fig. 40, young form showing a separate mass of chromatin posterior to the nucleus.

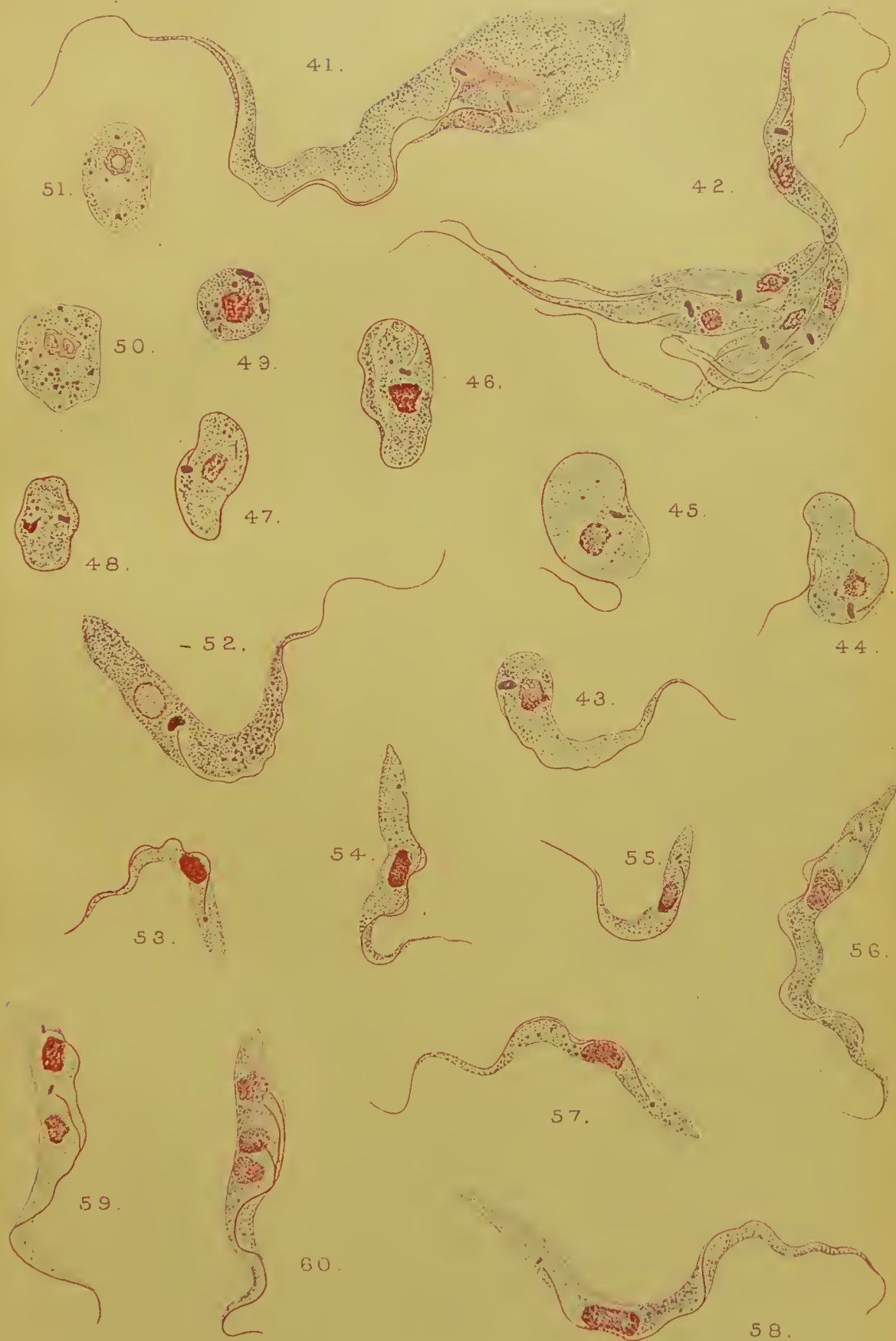
PLATE 3.

Trypanosoma grayi, figs. 41-52; *Trypanosoma tullochii*, figs. 53-60; all from the gut of the tsetse fly (*Glossina palpalis*). Fig. 41, very large female form, undergoing unequal division from a fly which had not fed on blood. Fig. 42, rosette-like mass of similar young forms. Figs. 43-51 are all taken from the same fly, and show the various steps in the formation of circular non-flagellated forms from a common type. Fig. 43. Figs. 44 and 45 show the flagellum becoming wrapped round the body of the parasite. Figs. 46, 47 and 48 show progressive stages in the absorption of the flagellum. Figs. 49, 50 and 51 are different types of the resulting non-flagellated bodies. Fig. 52, an uncommon type of parasite, with very large blepharoplast, and showing much chromatic granulation, from a fly which had not fed on blood.

Figs. 53-60, *Trypanosoma tullochii*. Fig. 53, small form, with minute circular blepharoplast and small vacuole. Fig. 54, larger form of a similar type. Fig. 55, small form showing the flagellum arising from a small granule of chromatin close to the blepharoplast. Fig. 56, large form. Figs. 57 and 58, large forms of trypanosome found in the proventriculus of an infected fly. Fig. 59, dividing form, common type. Fig. 60, dividing form, rare type showing division into three. Figs. 53-60 are all from the same fly. Figs. 57 and 58 are from the proventriculus, while the remainder are from the gut of the fly (*Glossina palpalis*).







22. ON THE OCCURRENCE OF ENCYSTATION IN *TRYPANOSOMA GRAYI* NOVY, WITH REMARKS ON THE METHOD OF INFECTION IN TRYPANOSOMES GENERALLY.

By E. A. MINCHIN, M.A.

[Reprinted from PROCEEDINGS OF THE ROYAL SOCIETY,
SERIES B, VOL. 79.]

In a tsetse-fly dissected and examined by me in the laboratory of the Sleeping Sickness Commission at Entebbe, Uganda, it was found that not only was the intestine swarming with *Trypanosoma grayi*, but the proctodæum also contained vast numbers of trypanosomes. Under moderate magnification they could be seen in dense clumps attached to the wall of the proctodæum, each clump having a superficial resemblance to a patch of mould, the whole mass, however, vibrating with the movements of the flagella. It was rather uncommon to find these parasites in the hind gut, and I at once made smears from different regions of the digestive tract, and carefully preserved and stained them. As it was but a short time before my departure from Entebbe, I was not able there to do more than glance at my preparations, but I noticed at once an important fact which, since my return to England, I have been able to confirm and extend by careful study of my slides: namely, that in the hind-gut the trypanosomes are in process of becoming encysted. Before proceeding to describe the encystment, I will say a few words about the conditions of the occurrence of these trypanosomes, and the manner in which they were preserved.

The tsetse-fly in question was one of a batch caught by our fly-boys at Entebbe on November 2, and fed the next day on a monkey infected with *Trypanosoma gambiense* from the cerebrospinal fluid of a sleeping sickness patient. On every subsequent day these flies were fed on a healthy guinea-pig, and a certain number of flies were dissected daily and examined, until the batch was used up. Without going into details it is sufficient to say that *T. gambiense* was found sparingly in the flies dissected up to 96 hours, that is to say, on November 4, 6, and 7. After this date *T. gambiense* disappeared completely and could not be found in any of the flies dissected. The fly in which the encystment was discovered was dissected on November 14. It must, of course, have been infected with *T. grayi* when caught, and, as I have stated, it had been kept 11 days in the laboratory and fed daily. At the autopsy it was found to be gorged with blood, and with all its organs perfectly normal and healthy in appearance. I examined the salivary glands and genital organs (tsetses

and vesiculæ seminales) without finding anything resembling a trypanosome. Finally the digestive tract was examined with the results stated. No trypanosomes were found in the proventriculus.

The films were made in the usual way by drying the smears, which were then fixed with methyl alcohol and stained with Giemsa's stain. A few were kept unfixed and have been fixed and stained for me recently by my assistant, Dr. J. D. Thomson, with excellent results. It is a matter of great regret to me now that none of my smears of this fly were fixed by the osmic-vapour-method. The method of drying smears is a drastic one, which is likely to deform finer details, and in the present instance the cyst-wall is often injured, being evidently of a soft consistence.

The gut was divided into four regions and smears made from each. In the anterior region of the intestine the ingested blood is of red colour, very thick, and jelly-like and difficult to smear out nicely. Further back it gets more fluid and begins to turn black. In the hinder part of the intestine the blood is black and fluid. I refer to these three regions briefly as the red, red-black, and black blood respectively. The black blood stops sharply and suddenly at the point at which the Malpighian tubules enter the gut. The proctodæum contains no blood, but only a yellowish fluid containing innumerable coarse granules.

I proceed now to describe briefly the process of encystation observed by me in the fly. A glance at the preparation shows many different stages of the process side by side. In the first place we find individuals in which encystment has not begun (figs. 1, 2). These are forms for the most part very slender and smaller than any of the forms of *T. grayi* found in the intestine of this or other tsetse-flies; but their most striking feature is the absence of any distinct undulating membrane, so that they bear a great resemblance to the genera *Herpetomonas* and *Crithidia*, especially the latter. The flagellum is long and appears to run down the side of the body. The blepharoplast has the large size and rod-like form characteristic of *T. grayi*. The nucleus is either compact or broken up into granules of chromatin. Division stages have been found, but are very rare.

In the first stages of encystment the flagellum becomes shortened and stains more deeply, suggesting that as it diminishes in length it becomes thickened. At the same time the cyst begins to appear as a layer of substance which stains reddish with Giemsa, forming a cap at the hinder pole (figs. 3, 4). These two processes continue until on the one hand the flagellum is completely retracted and on the other hand the body is enveloped in a pear-shaped cyst, at first incomplete towards the pointed end (figs. 5, 6). The flagellum appears to become retracted into a pink-staining vacuole (fig. 5, *fl. v.*), which reminds one of the flagellar vacuole described by Leishman

during the formation of a flagellum in the Leishman-Donovan bodies in cultures, but here the sequence of events is inverted, as it were. Finally the pink vacuole disappears, but a streak, which gradually fades away, can be seen for a time in front of the blepharoplast (fig. 6). The cyst closes up round the pointed end of the body, and then changes in form, becoming first oval (fig. 7) and then irregularly circular in outline (fig. 8). In the circular cysts, which are the last stage, it is difficult to make out much detail, but in favourable examples they can be seen to contain hyaline protoplasm, staining faintly bluish, with the dark purple-stained blepharoplast and the nucleus generally represented by irregularly scattered granules, staining a purplish-red tint. The cyst-wall also stains strongly and appears slightly redder than the nucleus.

I will now state briefly the conditions observed in other parts of the gut of the fly in which the cysts were found. The red blood was found teeming with trypanosomes, nearly all large forms of indifferent type. Very few young forms were found, and male forms were very scarce. No pronounced female types were found in this region, though many of the large indifferent forms approach the female type in the shortness of their free flagellum. In the red-black blood the conditions were similar, but young forms are becoming commoner. In the black blood young forms predominate and large individuals are comparatively infrequent. Thus in the gut of this fly as a whole we find great rarity of differentiated sexual forms, but a swarm of indifferent forms which in the hinder part of the intestine give rise to very numerous young forms, and these in their turn would appear to pass into the small, *Herpetomonas*-like forms found in the proctodæum, starved-looking creatures which, in a medium where there is probably no nutriment, go through the process of encystment already described.

Having so far confined myself strictly to matters of fact, I will now offer a few suggestions and speculations as to the probable significance of the encystation in the economy of the life-cycle of the parasite. In the first place, the resemblance of these cysts, and especially the pear-shaped forms, to the "Schleim-cysten" described by Prowazek* in *Herpetomonas muscæ-domesticæ* Burnett, is very marked, and has struck everyone to whom I have shown both my preparations and Prowazek's figure. I think there can be no doubt that they are similar bodies, and have a similar function, that is to say, that they are destined to pass out of the gut of the fly with its dejecta. Very numerous analogies in support of this inference could be cited from other parasitic Protozoa. The question which interests us most is, what becomes of them after being cast out from the fly? In the absence of any observations or experiments upon this point, one can only draw conclusions from the analogy of what is known in other cases. In the case of *H. muscæ-domesticæ*, the

* "Arbeiten a. d. k. Gesundheitsamte," Berlin, vol. 20 (1904). p. 446.

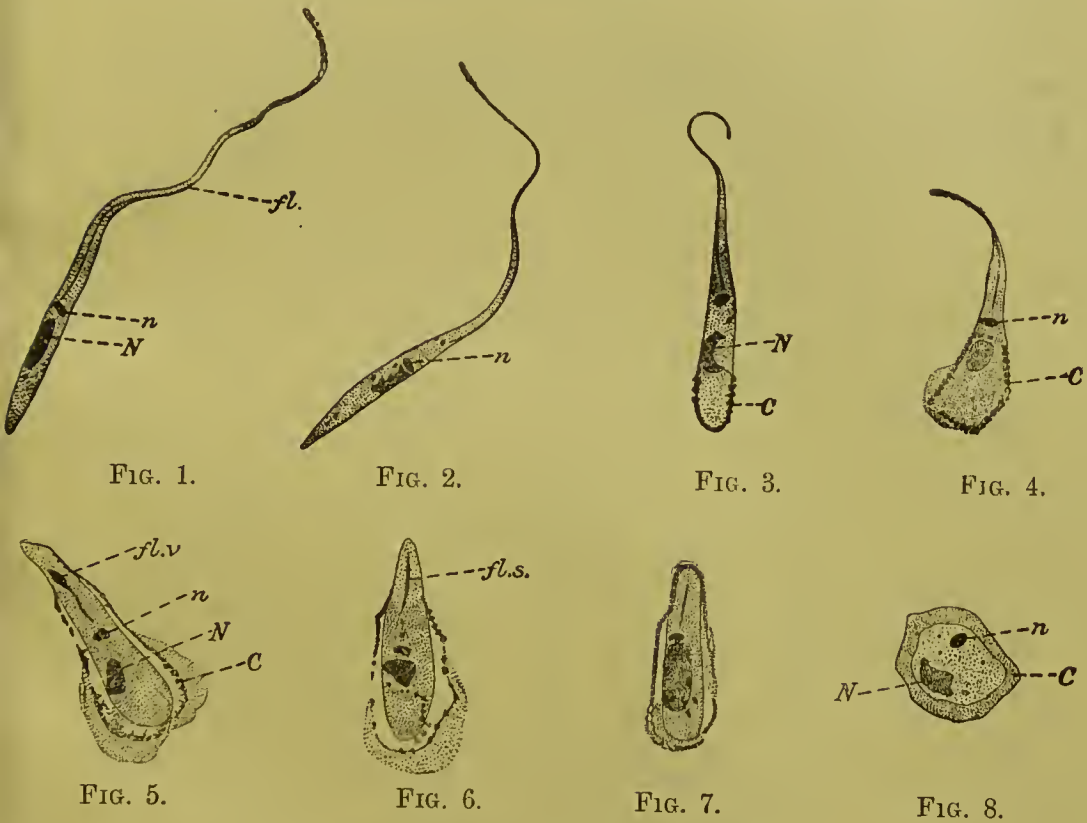
cysts are scattered about everywhere, and as house-flies are far from being particular in their feeding or sanitary in their habits, a fly runs every chance of infecting itself with the *Herpetomonas* by swallowing with its food cysts dropped by another fly. There can be no doubt whatever, it seems to me, that this is the manner in which the house-fly acquires the infection of the *Herpetomonas*. The case is, however, very different with the tsetse-fly, which does not haunt the enclosed spaces and insanitary surroundings of the house-fly, but lives a free, open-air life by lake and forest. Nor is the tsetse-fly a foul feeder like the house-fly. My assistant, Mr. Degen, and myself made many attempts to feed tsetse-flies on all kinds of food, but always without the least success. On the other hand, the tsetse-fly is a greedy blood-sucker, and will attack anything from a frog, lizard, or bird to a hippopotamus, but, in my opinion, it does not feed in any other way. Further, the tsetse-fly is not like the *Stomoxys*, which lays its eggs in dung; it is viviparous, as is well known, and nourishes its larva in the uterus until full-grown.

For all these reasons, it seems to me in the highest degree improbable, indeed, I may say impossible, that a tsetse-fly would ever infect itself by sucking up cysts dropped by another fly, or that a parasite which had to depend on this method of dissemination could maintain its existence in the tsetse-fly. The only possible destiny I can imagine for these cysts is to be swallowed accidentally by some vertebrate, the (as yet unknown) host of *Trypanosoma grayi*, in order to germinate in its digestive tract, to pass thence into the blood, and to be taken up again with the blood by the tsetse-fly. A cycle of this type is as yet unknown, but there are abundant analogies for all parts of it. In the first place, it is a common thing for animals to have protozoan parasites in the gut, which they take up in the encysted condition after they have been dropped by another individual. Without multiplying instances unnecessarily, I may point out that Schaudinn proved the infection of *Amœba coli* to originate in this way, and that it is a common human parasite in regions where sanitation has not advanced beyond the primitive condition of *épandage par terre*. In the second place, there are many instances among Sporozoa of cysts germinating in the intestine and liberating motile forms which then pass through the wall of the gut into other organs of the body.

In a former communication by my colleagues,* Lieutenants Gray and Tulloch, and myself, we were able to confirm Bruce's results as to the existence of direct mechanical infection by means of the tsetse-fly, which if it stabs its proboscis first into an infected animal and then soon after into a healthy one, can infect the latter. We were not able to demonstrate, however, what I may term cyclical infection, which at present has not been shown

* "Roy. Soc. Proc.," vol. 78 (1906), p. 242.

to exist. I suggest that there are two possible modes of cyclical infection, in the dissemination of protozoan blood-parasites by biting insects generally. In one method, which I may term *inoculative*, the parasite, after going through developmental changes in the insect, passes back again into a second vertebrate host through the proboscis, as in the case of malaria transmitted by a mosquito. In the other method, which I propose to term *contaminative*, the parasite taken up by the biting insect, after going through developmental changes within its gut, would pass



DESCRIPTION OF THE FIGURES.

FIGS. 1 and 2.—Free-swimming *Herpetomonas*-like forms of *Trypanosoma grayi* from the proctodæum of the tsetse-fly, before encystation has commenced; *N.*, principal nucleus; *n.*, blepharoplast; *fl.*, flagellum. $\times 2,000$.

FIG. 3.—Commencement of encystation. The flagellum is becoming retracted, and the first appearance of the cyst-secretion is seen at *C*. $\times 2,000$.

FIG. 4.—Similar stage slightly more advanced. The cyst-wall (*C*) is damaged at one point. $\times 2,000$.

FIG. 5.—Flagellum completely retracted, represented by a vacuole (*fl. vac.*). $\times 2,000$.

FIG. 6.—The flagellar vacuole is absorbed and the flagellum is represented only by a delicate streak (*fl. s.*). Cyst much damaged. $\times 2,000$.

FIG. 7.—The cyst-secretion now extends all round the body. $\times 2,000$.

FIG. 8.—Rounded-off cyst, the final stage. Letters as before. $\times 2,000$.

out of it through the anus, and infect the vertebrate host by contaminating its food or drink. We have all of us (I speak for myself) been imbued hitherto with the idea that the cycle of the trypanosome in the tsetse-fly must be of the inoculative type and have failed to find it. I wish to suggest strongly to those working on the subject of trypanosome-infection the desirability of making experiments and observations to prove or disprove the existence, in the insect which disseminates the parasite, of a life-cycle which results in a contaminative infection of the vertebrate host.

A full account of the trypanosome-cysts described in this note, and of other points relating to *Trypanosoma grayi*, will be published, with illustrations, in the "Quarterly Journal of Microscopical Science."

REPORTS
OF THE
SLEEPING SICKNESS COMMISSION
OF THE
ROYAL SOCIETY.

No. IX.

LONDON:
PRINTED FOR HIS MAJESTY'S STATIONERY OFFICE,
By DARLING & SON, LTD., 34-40, BACON STREET, E.

And to be purchased, either directly or through any Bookseller, from
WYMAN AND SONS, LTD., FETTER LANE, E.C. ; or
OLIVER & BOYD, TWEEDDALE COURT, EDINBURGH ; or
E. PONSONBY, 116, GRAFTON STREET, DUBLIN.

1908.

Price One Shilling and Sixpence.



REPORTS
OF THE
SLEEPING SICKNESS COMMISSION
OF THE
ROYAL SOCIETY.

No. IX.

LONDON:
PRINTED FOR HIS MAJESTY'S STATIONERY OFFICE,
By DARLING & SON, LTD., 34-40, BACON STREET, E.

And to be purchased, either directly or through any Bookseller, from
WYMAN AND SONS, LTD., FETTER LANE, E.C. ; or
OLIVER & BOYD, TWEEDDALE COURT, EDINBURGH ; or
E. PONSONBY, 116, GRAFTON STREET, DUBLIN.

1908.

Price One Shilling and Sixpence.

CONTENTS.

	PAGE
23. Report on Sleeping Sickness in Uganda from January 1st to June 30th, 1906. By A. D. P. Hodges, M.D. Lond. (With Introduction by Lieut.-Col. J. Will, R.A.M.C., Principal Medical Officer, British East Africa and Uganda Protectorate)	3
24. Reports on the Sleeping Sickness Camps, Uganda, and on the Medical Treatment of Sleeping Sickness Patients at the Segregation Camps, from December, 1906, to January, 1908. (With Introduction by H.M. Commissioner H. Hesketh Bell, C.M.G., to the Secretary of State.) By Captain A. C. H. Gray	62
25. A Preliminary Summary of the Results of the Experimental Treatment of Trypanosomiasis in Rats. By H. G. Plimmer, F.L.S., and J. D. Thomson, M.B., C.M.	97
26. Further Results of the Experimental Treatment of Trypanosomiasis in Rats; being a Progress Report of a Committee of the Royal Society. By H. G. Plimmer, F.L.S., and J. D. Thomson, M.B., C.M.	107
27. Note upon Sodium Antimonyl Tartrate. By R. H. Aders Plimmer, D.Sc. Lond.	117
28. Index to the first Nine Reports of the Sleeping Sickness Commission of the Royal Society	119

23. REPORT ON SLEEPING SICKNESS IN UGANDA from January 1st to June 30th, 1906.

By A. D. P. HODGES, M.D., LOND., Medical Officer in Charge
of the Sleeping Sickness Extended Investigations.

INTRODUCTION.

By LT.-COLONEL J. WILL, R.A.M.C., Principal Medical
Officer, British East Africa and Uganda Protectorates.

The first half-yearly report of the Medical Officer in Charge of the Sleeping Sickness Extended Investigations, Uganda, is a valuable one, and reflects much credit on Dr. Hodges, the Medical Officer in Charge, for his energy and ability. Although no new discovery of any magnitude regarding sleeping sickness has been disclosed, it shows more definitely than has hitherto been done, the exact distribution of the *Glossina palpalis*, its relation to the spread of the disease, and indicates lines on which it is possible to control and diminish this fearful scourge.

In the early stage of investigation into sleeping sickness by the Royal Society's Commission under Colonel Bruce, clearing the fly-infested areas and thus destroying their natural *habitat* was proposed, but at that time the fly range was not defined, and was supposed to be more extensive than these recent investigations have proved to be actually the case. Indeed, it has now been shown that the fly range is very limited. Clearing such areas as are suggested in this report may, therefore, now be considered as practical, and a much less onerous and expensive undertaking than was at first supposed.

Segregation of infected cases had also been proposed from time to time, but the proposal was met with passive resistance by the natives, probably influenced by their chiefs, who may have been apprehensive of a decrease in their personal revenues following on the removal from their holdings of a large number of their tenants.

It is satisfactory to note that in every locality where these investigations were made, the Medical Officer was received with a degree of confidence, which not only speaks well for the tact of the officers employed on these investigations, but is promising for the success of any measures which the Administration may introduce in dealing with the disease.

I consider that segregation and clearing are the most important and practical measures that can be adopted in the present state of our knowledge, but would also strongly advocate an extensive trial being made in treatment by means of atoxyl.

I may mention that while visiting the Imperial German Government's Commission on Sleeping Sickness at Sese, I was shown several cases of sleeping sickness in which a very marked improvement had been effected by the administration of atoxyl; and Professor Koch, under whose able direction that Commission is working, informed me that, judging by the results he had so far obtained, he was very hopeful of the success of this drug. In this connection I may further mention that I have recently been in communication with Dr. E. van Campenhout, of the Belgian Colonial Hospital, Watermael, who some months ago published notes of three cases and his method of treatment, and who states that his cases, which were in a fairly advanced stage of the disease, are now apparently cured.

Dr. Bagshawe's discovery of the pupæ of *Glossina palpalis* is important, insomuch that it may be possible to destroy the young of the tsetse fly, by introducing and protecting birds who collect their food by "scratching," *e.g.*, guinea-fowl, spur-fowl, &c.

I. FIRST HALF-YEARLY REPORT of the MEDICAL OFFICER IN CHARGE OF THE SLEEPING SICKNESS EXTENDED INVESTIGATIONS to the PRINCIPAL MEDICAL OFFICER, East Africa and Uganda Protectorates. BY DR. A. D. P. HODGES.

On January 20th, 1906, I arrived at Entebbe from Gondokoro to take charge of the Sleeping Sickness Extended Investigations, and on January 22nd I met Lieutenant-Colonel Will, the Principal Medical Officer, there to learn what was intended in the proposed scheme and to receive general instructions as to what was to be undertaken. I also saw the correspondence on this subject which had passed between the Royal Society and the Colonial Office.

I at once drew up a short programme for the conduct of the investigations, which met with the Principal Medical Officer's approval and that of the Acting Commissioner, and on January 29th I completed the draft of my general instructions to the Medical Officers (see Appendix), who were to be under my direction, but, owing to pressure of work at the Government Printing Office, these instructions were not available for circulation until February 20th.

On January 29th the first Medical Officer, Dr. Wiggins, arrived from East Africa, and proceeded to Usoga, which had been allotted to him as his sphere of investigation. On February 5th, Drs. Van Someren and Uffmann arrived, the former proceeding immediately to investigate the district of Kampala and the lake region south of it, while the latter, after a few week's delay in Entebbe, in order to make himself

familiar with sleeping sickness, the fly, the trypanosome, and the technique of examination, proceeded to carry out his enquiries in the country bordering on the lake shore between Entebbe and the Usoga boundary, including Bugerere. Dr. Densham, to whom was allotted the Nile Province, was then in medical charge of Nimule Station, and was unable to finally hand over to his successor until March 12th, soon after which date he proceeded to investigate the northern limit of *Glossina palpalis* on the right bank of the Nile. Dr. Bagshawe also, who was to examine the south and west of the Protectorate, was in medical charge of Hoima, and was not available for his new duties until March 31st, a few days after his relief arrived.

On April 1st I took over charge of the staff, the patients, and the stock of animals left by the Sleeping Sickness Commission of the Royal Society, and on April 14th I took over also the duties of Senior Medical Officer from Dr. Moffat. Unfortunately at this time, and for three months onwards, an abnormal and unprecedented wave of sickness, consisting chiefly of malaria and dengue fever, passed over the country, and prevented any opportunity of personally inspecting, as I had hoped to do, the investigations of the Medical Officers; but I am glad to record that the general satisfactory nature of their reports precludes any regret on that score.

The period under review then, in this report, is roughly six months, from the commencement of operations till August 31st, 1906.

My main object has been to obtain in the first place an accurate knowledge of the distribution and habits of *Glossina palpalis*, and, whilst doing this, to gain the confidence of the natives, so as to be able the more easily and profitably to apply later on the preventive measures which might appear advisable, and any form of treatment which might in the meantime or in the future be discovered.

The result is so far satisfactory that a sufficient working knowledge of the distribution of the fly for practical purposes has already been obtained, and though, as regards its habits, there are still important details to be learned, I believe that in future its distribution will need investigating only in special places and for special purposes. I think I may also say, judging from the general reception of the Medical Officers, the increased interest shown in their proceedings, and the notice taken, in many places, of their recommendations, that the confidence of the natives in our motives and methods has been so far increased as to render the application of any general measures much more likely to be successful, in many parts of the Protectorate, than has been the case in the past, when the general attitude has been one of suspicion and passive resistance, or, at the best, indifference.

In framing my general instructions to the Medical Officers, the two measures most in my mind were segregation of the sick and clearing of the jungle in those haunts of the fly near to human dwellings and on traffic routes, and I was anxious to follow up, and, if possible, confirm the observations which I had made in Unyoro and the Nile Province,* especially those which seemed to me to afford the hope that in some form or other either or both of these measures might prove capable of successful application.

I consider that we now possess sufficient knowledge of the distribution of sleeping sickness and of the fly to enable us to say with certainty what places it is most important to clear, and to judge with a fair amount of accuracy to what extent the clearing should with advantage be carried; while we can also decide definitely from what localities the sick should be removed and to what localities they can be removed with absolute safety to the community as regards infection.

Hitherto the results of clearing as it affects the fly have not been well understood, nor has it seemed to be realised to what extent and in what localities it was most urgent. And, in particular, confusion of ideas has existed as to what constitutes an "infected locality," so that it will be well at once to state definitely what the term might be supposed to include, and also what is meant by it in this report.

An infected locality as regards the fly is a fly-range or series of fly-ranges which, directly or indirectly, by settlement or communication, is in contact with a place or places in which there is sleeping sickness, and it will remain infected so long as it is in contact with such places, and, if contact be cut off, so long as infection endures in the fly, which is at present an unknown quantity. It is, therefore, a circumscribed area, consisting of a narrow strip from a few yards to a few miles in length, along a lake shore or river bank, in which area the disease is communicable to man, and in which the duration of infection, after all infected vertebrates have been removed, is at present unknown.

An infected locality, as regards human beings, on the other hand, may be of very much wider extent, and in it the disease is *not catching*, except where it coincides or comes in contact with the fly-ranges (which form, as a rule, a very small proportion of it). I think, therefore, that it would be better, for the sake of clearness, to use the term "infective" to describe the former locality and to retain the term "infected" for the latter only.

It is these "infective localities" which need to be destroyed, wherever practicable, by clearing; and it is from these localities and from communication with them, where their destruction by clearing or otherwise is not practicable, that it is necessary to remove the sick.

* Since published in Report No. VIII.

Segregation has been more than once brought forward as a general measure, but rather in the form of a prolonged quarantine, and, owing to the uncertainty felt with regard to finding safe locations for those who were to be segregated, and also as to the exact localities from which all the sick should be removed—owing, in fact, to the impossibility of forming any clear idea as to the necessary extent of the undertaking—the plan has been abandoned.

I hope to be able to show, in the course of this report, that neither of the above measures, extensive though they both may be, is of nearly so vast a magnitude as has been feared, and that, whatever difficulties may stand in the way, their application in some form or another should, if any effort at all is to be made, be begun without further loss of time and while there yet remains the possibility of saving many lives.

With regard to sleeping sickness and its distribution, little has been added to our former knowledge, and, except for a gradual extension northwards in the Nile Province, which may be an extension only as regards our knowledge of its existence there (see below), it remains practically *in statu quo*. On the whole the reports seem to show that cases are considerably less numerous than formerly, probably on account of the large proportion of the inhabitants of the worst localities who have already died, and of the fact that many of the survivors from these places have fled inland. The disease has been everywhere found to be most closely associated with the fly, and apparently there has been no difficulty in deciding that all cases found at a distance from the haunts of *Glossina palpalis* are “imported” ones.

On my way from Gondokoro in December, 1905, to assume charge of these investigations, I found sleeping sickness to be epidemic at two places on the Nile bank midway between Nimule and Wadelai. At both these places fly was present, and at neither was there a customary camping-ground for travellers. It was evidently not a very recent introduction, and the Medical Officer who has since investigated there reports it to be of at least four years’ standing in that region. In my former report I recorded the fact that *Glossina palpalis* was present on most of the inland streams north of the Victoria Nile, and probably on all, wherever the conditions of open water, shade, &c., were favourable to it. This particular part, however, I was unable to examine, except at the two places at which the steam-launch touched, which carried me from Wadelai to Nimule. It is, in fact, a part seldom traversed on land by officials, and then always as rapidly as possible, owing to the great difficulty in obtaining porters; and that appears to be the reason why the disease failed to come under notice earlier. Moreover, there, contrary to what obtains at most other places, the fly, and therefore sleeping sickness also, is much more plentiful on the inland streams

than on the Nile itself, on which, indeed, it is rarely found in this part of its course, at least on the Uganda side. Inter-tribal communication is free, both inland and across the Nile, on both sides of which the disease exists, and, though the population is far from numerous and the villages are scattered, I fear there is little hope but that the infection will eventually spread as far as the northern limit of the fly, which is, on the right bank, some 40 to 50 miles south of Gondokoro. There is, however, little chance of an epidemic of the magnitude of that of the Victoria Nyanza.

A small and circumscribed epidemic was found by Dr. Wiggins to exist between Usoga and Mount Elgon, and will be referred to later. The genuineness of the epidemic reported to exist some time ago on Lake Albert Edward is open to serious doubt, as will be seen below. It is probable that it may turn out to be beri-beri or, perhaps, both this disease and sleeping sickness may be present, since the fly, at any rate, is plentiful there. Unfortunately it has been impossible hitherto to investigate it thoroughly, owing to political reasons.

I did not anticipate that the Medical Officers, who have been constantly travelling, would be able to do very much in the way of microscopical investigation and experiment, but accounts of some ingenious and interesting experiments by Dr. Bagshawe on the flight of *Glossina palpalis* along river banks are given, and also a report by Dr. Van Someren on the presence of *Trypanosoma gambiense* (?) in naturally-infected native dogs.

Incidentally, I have caused enquiries to be made into the existence in the Uganda Protectorate of the fly *Auchmeromyia* and its larvæ, the Congo—or floor-maggot, and it seems likely that *Auchmeromyia luteola*, and possibly other species, will be found to be widely distributed, but the identification of specimens is not yet complete.* Also a disease (or diseases) called by the natives ruhinyo, muhinya, enya-nya, and bihimbo, the names being, apparently, used indiscriminately and interchangeably, has received attention. An epidemic called by one or more of these names had been reported from Ankole, and, when Dr. Bagshawe arrived at Lake Albert Edward to investigate the epidemic there, about the only facts that he could gather were that there certainly was an epidemic, and that it was called ruhinyo.

Since, therefore, ruhinyo or muhinya has been rumoured to exist in the interior of Toro as well as in Ankole, and I had already instructed Dr. Lowsley, the Medical Officer of the latter Province, to investigate it there, Dr. Bagshawe was at once directed to examine the inland epidemic of Toro. Dr.

* Report since received from Mr. E. E. Austen, British Museum. The fly or maggot of *A. luteola* has been collected in Uganda, Usoga, Unyoro, and the Nile Province.

Bagshawe thinks, and I agree with him, that there is little room for doubt that the epidemic which he then examined is beri-beri, a disease new to our experience in this country.

I had hoped that an enquiry as to whether *Glossina morsitans* and other tsetse flies can convey *Trypanosoma gambiense* could have been commenced ere this, but it has been found necessary to postpone it. It will, however, in all probability be undertaken shortly.

It is a matter of very grave importance, and especially so in the Nile Province, where, as I found during my term of residence, both *Morsitans* and *Pallidipes* are present, and, in some places, abound. They are to be found, probably co-extensive, from Northern Unyoro to the northern border of the Protectorate, and how far beyond this I am unable to say, but they become more plentiful just where *Glossina palpalis* has its limit, and, if unfortunately they can convey the infection, the epidemic may spread into the Sudan. My own belief is, however, that they will not prove to be natural carriers.

In my previous report I pointed out that there is no continuous "fly-belt" across the Uganda Protectorate, but the *Glossina palpalis* exists in certain circumscribed strips or narrow patches along the margins of lakes, rivers and streams. These areas I propose to call "fly-areas," and the limit of flight from the waterside at such places the "fly-range," reserving the term "fly-belt," which has been very loosely used, and had no well-defined meaning, to describe the limits of distribution across the continent. I have already used these terms above and I propose to adhere to the definitions throughout this report.

I also showed that the fly-areas and fly-ranges, both of which are local and vary with the locality, are much narrower than had previously been supposed; that, far from inhabiting swamps, the fly rather avoids them, and is absent or scanty on the true shore, even if shaded, behind wide belts of swamp, while it is practically never met with on swamps pure and simple nor on swamp-filled rivers and streams (which I shall call hereafter, for the sake of brevity, "swamp rivers"); that the conditions most suitable to them are open water, however small in extent, contiguous shade and a certain amount of raised or definite bank. I recorded also the fact that *Glossina palpalis* was present on most or all of the inland streams which are open, with running water, wherever there was sufficient shade, and that, in the case of very narrow streams, this might be afforded sometimes by high or over-hanging banks or even by long grass.

I described how it is probable that in most cases sleeping sickness is conveyed from place to place by man, especially along main traffic routes, and from man to man, in suitable localities, by the fly; how in any epidemic area the local intensity of infection varies with certain physical and geo-

graphical conditions such as indented coastline, peninsulas, islands, rivers, swamps, shade, cliffs, open water, &c., which affect the fly, and how these conditions again interact with others, which chiefly concern the human inhabitants, to determine the magnitude of an epidemic and the direction of its spread, these last conditions being, chiefly, density of population, relation of dwellings and occupations to local fly-ranges and the methods and frequency of intercommunication; and I showed how certain localities within or in contact with fly-ranges are reciprocally infective, while others, beyond the fly-range, can be infective only *via* the fly-ranges, the chances of the spread of infection varying with the distance therefrom and the frequency and facility of communication therewith; also that it is possible for settlements well outside the local fly-ranges, if so situated as to be in frequent and easy communication with them, perhaps on several sides (as often happens in an island or a peninsula), to show a very high percentage of infection among their inhabitants, although the transmission of infection is impossible within their precincts, and I attached diagrams to illustrate these points and also to show the probable method of extension of the Lake Victoria epidemic, the most probable connection between it and the Lake Albert and Nile epidemic and the probable direction of spread in the near future.

I will now give a short summary of what the various Medical Officers engaged in the extended investigations have recorded.

All agree that the haunts of *Glossina palpalis* are close to open water with shade, especially that of undergrowth and scrub. Dr. Bagshawe notes that the banks are often steep and generally have a decided slope. Dr. Densham mentions that most of inland streams on which the fly abound (which are always open, flowing streams) have steep or definite banks. Dr. Wiggins describes a peculiar distribution on the Mpologoma River (which is so extensive that it more nearly resembles a great lake, the greater part of which is choked with sudd), where fly is absent on the numerous creeks, which run inland often for miles, choked with swamp and having no definite banks, while, in the few places where it is present, it is found on the true shores or those parts or points nearest the main body of the lake where, in all probability, the banks would be comparatively firmer and higher and there is more likelihood of the existence of patches or strips of open water at the sites of ferries, landings and dipping-places. Dr. Van Someren describes one of the few inland streams in his district on which fly was present as having very well-defined banks. We may take it, then, that the essentials of a typical fly-area are more or less open water, with contiguous and especially overhanging shade, preferably of scrub (though in very narrow streams high banks or even high grass may be sufficient), and a certain amount of fairly well-defined bank or shore, this last being essential, in all probability, for the breeding-grounds.

All the Medical Officers agree as to the absence or only occasional presence of fly on the true shore behind wide belts of papyrus or other luxuriant and close-growing swamp-vegetation, even though this shore may be well shaded and otherwise favourable to it, but they differ as to the width of such a belt necessary to ensure its absence. Dr. Van Someren found in his district that 30 yards and upwards was sufficient, and that flies are seldom seen either on the lake or shore side of such a belt, while the only width of belt mentioned by Dr. Wiggins behind which fly was absent is 100 yards. No doubt the necessary width varies in different localities and with other factors—such as the abundance of flies, the amount and kind of food supply, the existence of canoe or other traffic through it with neighbouring fly-areas from which a certain number might be “imported,” and with the length or extent of the belt along the shore or bank.

All are agreed that if, as occasionally is the case, especially where the sudd or swamp has floated in from elsewhere and has not grown out from a low, swampy shore, there remain patches or strips of open water at the true foreshore behind the swamp-belt, fly may be found at these places if the other conditions are favourable to it, but that on the outer margins of even a moderately wide belt the fly is not found. Narrow belts of papyrus or other such vegetation are not antagonistic to the fly, nor are open reeds, nor other small or sparsely-growing water-weeds. I may add that the presence of ambatch-bushes at the true shore or in the water near it, since other vegetation seldom penetrates them to any great extent, always means the existence of a little comparatively open water, and is thus favourable to the fly, but by no means an invariable sign of its presence.

All are agreed that *Glossina palpalis* does not exist on swamp-rivers; and it is either absent or very scanty on the swampy parts of comparatively open rivers. Since practically all the inland waters of Uganda proper, Buddu, South and East Unyoro, and Western Usoga are of this nature, the very important fact remains that practically the whole interior of these regions is fly-free, and therefore “safe,” country. The only notable exception to the above rule is part of the main trunk or basin of the Mpologoma which, as has just above been mentioned, is really a lake. There are also streams in South Usoga, apparently of a swampy nature, on some of which fly was found. It is not, however, clearly stated whether patches of open water existed in their course, but only that thick, overhanging shade and dense surrounding jungle were the rule upon their banks. Further, they were examined under the abnormal and most unusual conditions of flood and lake-level, referred to elsewhere. Dr. Uffmann records the presence of fly on streams near Munyonyu which were narrow and edged with papyrus, but with a clear central channel over-hung by shade. In my own experience the smallest trickle of a forest-stream is

more likely to harbour fly than acres of stagnant swamp or miles of swamp-choked river.

Several of the Medical Officers give as their experience that the fly is absent from cleanly kept native banana plantations unless these abut directly on a water side, and that, even then, they are usually seen only at the edge of the plantation nearest the water. This accords entirely with my own observations, which showed that banana plantations 20 or 30 yards from the water, if there is little or no intervening bush or scrub, are safe, and that bananas by themselves, unless at the water's edge, do not afford sufficient cover for the fly. Small patches near the water and shut in by dense forest or jungle, or placed directly between this and the water, are, however, most dangerous.

Drs. Bagshawe, Van Someren, and Uffmann specially note, and I have often observed myself, the absence of fly along the shore at the open grassy spaces which form breaks in the jungle or forest-fringe of lake or river, and that at such spaces, even when comparatively narrow, there are definite gaps in the distribution of the fly. The two former note its absence both on the lake-shore and also at the forest edge, when the forest is separated even by only 20 or 30 yards of clear ground or moderately short grass from the water, and this observation also I can confirm. It is important in clearing to remember that the long-shore range is naturally, and can be artificially, limited by open spaces.

Dr. Van Someren describes one very curious and unusual condition under which *Glossina palpalis* was absent from the lake-shore. The Gwamba swamp, which is long and very narrow, stretches for some miles along the coast of Buddu, separating the beach, which is a thin, sandy strip of slightly higher level than the swamp itself, and over which the lake washes in rough weather, from the forest or jungle fringe inland by a distance which is often only from 20 to 40 yards. This beach consists of a shelving bank, on the top of which are scrub, small trees and grass, all of which the lake being open at this part and free from sudd, are favourable to *Glossina palpalis*, and yet it was never found either on the beach or at the forest edge except at a few points where there were many open pools in the intervening swamp. It is evident, therefore, that swamp, unless it contains open water and shade, is just as inimical to the presence of the fly as clear ground or open grass.

It was found that *Glossina palpalis* was never present in isolated patches of scrub or forest not contiguous with the water side, and I think it seems pretty certain that it is absent from all forest unconnected with lake-shore or river-bank unless such forest includes streams or open pools within its own precincts.

While the conclusions as to the habitat of the fly show little divergence, the recorded experience as to its local range, though varying a good deal, shows a satisfactory agreement with regard to its average extent, since no doubt one would naturally expect a greater local and seasonal variation of the range than of the physical conditions of the very circumscribed localities affected by the fly.

The average "natural" range (which term I will define presently) is put by Drs. Van Someren and Densham at 10-30 yards from the water, and the same distance over water to a passing or incoming boat, while Dr. Uffmann puts it at only 10 to 15 yards. Dr. Densham mentions that he has only once seen a fly in his camp, which was at the time 50 yards from the water, and that he has frequently attended to numerous sick natives in his various camps, at a distance of from 50 to 150 yards from water, without once seeing a fly, though he was always on the watch. On the other hand Dr. Bagshawe found by direct experiment, at one of the rivers running into Lake Albert Edward, that flies came from the water to a distance of 50 to 80 yards, in a very short time, and in fair numbers, and bit some of his porters whom he had placed at these distances. Dr. Wiggins, too, while in South Usoga, frequently found fly, at any rate in one neighbourhood, half a mile, sometimes a mile, and on one occasion two miles, from any known water, though in other parts of Usoga, *e.g.*, on the Mpologoma, Nile and a few inland streams, he found much the same average range as the other observers, namely, 10-20 yards. His observations in South Usoga, however, were made under such abnormal conditions as might not occur again for many years. Both Dr. Wiggins and Dr. Bagshawe have occasionally noticed *Glossina palpalis* in their camps or tents at distances of 300 yards or more from water, while Dr. Van Someren found fly at 300 yards from water on one occasion only, in a densely-wooded locality on the Sese Islands.

Dr. Bagshawe states, as a general rule, that wherever he has found a fly there has always been water, with overhanging shade, either on the spot or within 300 yards. All seem to be agreed that the distance which flies will follow from their haunts after their victims does not, as a rule, exceed 300 yards from water, though, on a few occasions, where they have found special facilities for shade, single flies have followed or been carried more than twice this distance.

The range over water seems to be much the same as on land, and Dr. Van Someren says that he finds 80 yards about the limit to which flies will "follow" or accompany a canoe from the water's edge. This is very likely true for the majority of flies, as it is also on land, but a few will follow for longer distances, while individuals, especially such as are gorged, may, if they can find shade where they can remain undisturbed, as under the unoccupied thwart of a boat or in various parts of a vessel of any size, be carried for great distances. It is very

unlikely, however, that, on a native canoe, where there is little shade and generally constant movement, flies would be carried more than a few hundred yards, and then it would be only occasional ones.

Several Medical Officers, and I myself also, have observed that *Glossina palpalis* can bite through clothing such as khaki or a flannel shirt, but they seldom attempt it, and much prefer feeding on the bare skin. No evidence has been adduced of their feeding on anything but vertebrate blood, with regard to which they are, so far as my observations go, omnivorous. Dr. Bagshawe has noted their abundant presence in regions where there were no crocodiles. There is general agreement that *Glossina palpalis*, though a lover of shade, is more active during bright sunshine and less so in dull, cloudy weather, while during rain and high wind it retires almost completely. It is also less active, and, unless in places where it is very numerous, seldom seen, before 8 to 8.30 a.m. and after 4 to 4.30 p.m., though no period of the day is entirely safe from it.

This confirms what I have previously recorded, and Dr. Van Someren mentions, in addition, that he has noticed a much decreased activity towards noon and lasting till 1 or 2 p.m. He also gives some interesting counts which illustrate what has just been said:—

7.30 a.m. No flies ...	Cloudy and dull	{ This count shows very well the influence of dull weather in the small number captured and these only in bright intervals.
10 to 10.30	... Two females six males	{ Sunshine at intervals.	
10.30 to 11	... Two females two males		
11.30 to 12.30 p.m.	Nil Heavy rain ...	

The following three counts were made at the same place on consecutive days:—

(1)			(2)			(3)		
Hour.		Flies Caught.	Hour.		Flies Caught.	Hour.		Flies Caught.
A.M.	A.M.		A.M.	A.M.		A.M.	A.M.	
7.45 to	8.45 ...	2	7 to	8 ...	4	7.15 to	8.15...	—
8.45 „	9.45 ...	7	8 „	9 ...	25	8.15 „	9.15...	4
9.45 „	10.45 ...	17	9 „	10 ...	5	9.15 „	10.15...	21
10.45 „	11.45 ...	24	10 „	11 ...	—	10.15 „	11.15...	11
	P.M.		From 9—10 dull and cloudy.				P.M.	
11.45 „	12.45 ...	6	About 10 rain began and the flies disappeared.			11 15 „	12.15...	9
	P.M.						P.M.	
12.45 „	1.45 ...	8				12.15 „	1.15...	} 5
Bright sunshine continued all the time.						1.15 „	2.15...	
						2.15 „	3.15...	3
						3.15 „	4.15...	—
						Sunshine with cloudy intervals.		

Owing to the situation chosen no direct sunlight fell on the place of observation after 3 p.m., when it was found that no flies were obtainable. These counts show fairly well the influence both of weather and of the time of day.

Investigations have also been made into the numerical proportions of male to female flies in various fly-areas, which varies greatly, and probably bears some relation to the breeding-season (if there be such), or to the proximity of the breeding-grounds, or to both. In most cases males have predominated, and Dr. Bagshawe is the only observer in whose experience the reverse was the case. He is inclined to think that females are more numerous where human (vertebrate?) blood is easily obtained, and that they wander further than do the males in search of food. Some figures which he gives seem to support this view, but nothing definite has yet been proved, and the sex of such flies as have been taken at unusual distances from water has been recorded in too few instances at present to be of any decided value though, so far, they seem to have been more often females.

I do not propose to relate here the deplorable ravages of sleeping sickness which have been recorded in their reports of certain localities by those Medical Officers who have examined the most highly-infected districts. The state of things existing in such places has already been sufficiently well described for the situation to be well understood; it is not materially altered with regard to them, nor do I think it is under-estimated at present, either in existing accounts or in the general impression which prevails among the public. I will only state here that, however great the past ravages and however high the existing percentage of infection (and in some of the worst localities I fear this is very high), recent investigations show that the "infective" areas, those areas in which the disease is communicable to man, are much more circumscribed than was supposed, while the "safe" or fly-free area in the Protectorate is very much more extensive than at one time it was dared to hope.

These are facts which are not only reassuring in themselves as limiting the possible area of epidemic, but are also distinctly favourable to the successful application of preventive measures.

I decided that it was of no immediate importance to collate, as I at first intended, elaborate statistics of cases, death-rate, percentage of present infection, &c., from the several districts which are being investigated. This would have been not only extremely difficult to carry out in the first instance among our native population, but would have involved a very great expenditure of time and labour which, I considered, could be for the time being more profitably employed, especially since no records exist of sufficient accuracy with which to make useful comparison, and I wished to concentrate our investigations at first on such points as might elicit or determine facts which appeared to be of more immediate practical value.

I saw, too, that if, as I had reason to hope and believe, the results of further investigation should favour the successful application of any form of segregation or deportation from infective areas, any such figures would, if collected, be rendered practically useless by the shifting of inhabitants entailed by such a measure. I consider that now, however, with our present knowledge, the time will soon arrive when such statistics must be collected. They should be as accurate as it is possible to make them, and should prove of the greatest value for comparing with similar figures which may be obtained later on, after the application of preventive or curative methods, or of both, for any given period. I should propose that they be taken only from one or two definite and not too extensive areas, which should be selected with regard to the reliability of the figures likely to be obtained in them, their existing conditions as regards sleeping sickness and fly-distribution, and the facilities which they offer for being dealt with by preventive and curative measures.

Sufficient time has not yet elapsed for the Medical Officers to be able to report the effects of the local clearings which have been, or are being, carried out in their districts, but sufficient practical knowledge has been gained of the effects of clearing at Entebbe, Jinja, and elsewhere, where some considerable time has elapsed since it was undertaken. Dr. Bagshawe, however, records the fact that the clearing of scrub for a space of about 100 yards by 50 yards on only one side of the ferry on the lower Mpanga River immediately banished all the flies, which were previously numerous, from the ferry itself, and this although all the large trees were left standing. This, no doubt, is a particularly favourable instance, and probably a success so marked would not be lasting in its completeness, but it nevertheless serves to show the immediate detrimental effect which clearing of foreshore or river-bank has on *Glossina palpalis*.

Dr. Bagshawe has collected *Glossina fusca* in the country bordering on the north and east of Lake Kafuru (Albert Edward), and Dr. Densham has collected *Glossina morsitans* from the neighbourhood of Nimule and *Glossinae pallidipes* and *morsitans* from between there and Wadelai. The localities will be found marked on the accompanying map (No. I.), and on another map, also attached, which I have compiled of the distribution of the several species of tsetse flies found in the Protectorate. (Maps Nos. II. and III.)

The general distribution of *Glossina palpalis* in the Uganda Protectorate will be best seen on the accompanying map, No. I., where it is recorded as accurately as is possible, and also that of sleeping sickness, which, most intense in the infected fly-ranges, radiates or shades off from these and penetrates inland to a greater or less distance, according to the prevalence, intensity and reaction on one another, at the corresponding coast or river-side, of the various conditions which I have previously

quoted from my former report as governing the spread of an epidemic (see Appendix E.).

I will now endeavour to deal with several points which remain to be explained or discussed in connection, chiefly, with the fly-range, which, it will be readily understood, is one of the most important factors to be considered in all measures of precaution or prevention used against sleeping-sickness.

I have already made use, above, of the term "natural range," and by this I mean the distance from the waterside within which the flies naturally wander in their search of victims on whom to feed, as distinguished from the much greater distance to which they will follow victims who have come in contact with them by the fact of having passed through their "natural range" or feeding ground. It may not, at first sight, seem important to distinguish between these but, as a matter of fact, a distinction becomes most important, for example, in carrying out such a preventive measure as clearing, for, as we shall presently see, if the natural narrow range be constantly borne in mind in its application, the wide "following" range may practically be disregarded.

In order to be followed by a fly for long distances, such as have been mentioned above, a person must first come in contact with it in its natural range and, conversely, a fly would never reach these long distances inland unless it had first found, within its natural range, a victim to follow. Let us take the case of a village, the water-supply of which is from a stream or lake at a distance from it of 300 yards. The village itself may be (and practically always is) well outside the natural fly-range, but, if there are fly at the dipping-places, a certain number will "follow" far enough to reach the village more or less frequently, and thus this is brought within the "following" range. Yet, in order to protect this village from fly, there would be no necessity for clearing a width of 300 yards from the water-side, since a clear space of 50 yards, or perhaps even half that width, would banish the fly from the natural range, so that they could then no longer be brought from the dipping-places (or from any other bank or fore-shore which had been cleared) to the village. Take, again, the natural range from any given fly-area or feeding-ground, say, at a ford. If you clear this fly-area, which is probably 20-30 yards wide, and so make it uninhabitable for the fly, or if you divert traffic from it to some fly-free ford near by, the corresponding "following" range, no matter how wide it has been, will now no longer exist, since persons crossing the cleared natural range or the new fly-free ford will no longer encounter flies which might follow them. In brief, therefore, in clearing or abolishing the natural range you also abolish the "following" range.

I have never myself seen *Glossina palpalis* more than half a mile from water, except where they were being brought in by natives, daily and in large numbers, for scientific purposes,

and there was the possibility of occasional escapes. Moreover, the few instances when I have seen it at this distance occurred at a station where the water-supply was half a mile away, and water was being constantly brought from a jungle-fringed, fly-infested shore. Those cases in which flies have been observed at considerable distances (from 300 yards to 2 miles) from any known water have, so far (apart from those reported as "following" flies), occurred only in the most thickly jungle-covered districts, such as South Usoga and the Islands, and usually under abnormal conditions of rain and flood. In some instances their presence has been explained by the discovery of forest-streams or pools near by, and it is possible that such hidden waters may have been present in other cases, but a proportion remains in which apparently there is no such explanation. I think there can be no doubt, however, that, wherever flies have been seen in considerable numbers, some pool or stream has existed near at hand.

Possibly the natural range, and certainly the "following" range, is increased in the wet season when the undergrowth is more luxuriant. The latter is also wider in thick jungle or forest and in dull weather, and narrower in the open and in bright sunlight.

I have elsewhere recorded (see Report VIII.) that, on approaching a fly-area, flies were rarely met with more than 50 yards from the water, but that, on leaving such an area, a few may follow for longer distances up to 300 yards. This latter and also somewhat greater distances have been recorded during the present investigations for following "flies," the "following," in the case of these longer distances, being generally through scrub or some sort of continuous or slightly intermittent shade. An artificial shade, such as an umbrella, a wide-brimmed hat or a pail of water carried on the head, will sometimes be taken advantage of by a fly, especially when gorged, and it might possibly remain in its retreat, if undisturbed, over a distance of several miles. All such cases are, however, exceptional, and only serve to account for the occasional observation or capture of flies in unusual or unexpected places.

The "following" range is, no doubt, also influenced to a great extent by the conditions of food-supply. For instance, at uncleared fore-shores, where there is frequent human traffic through wide belts of jungle, conditions which obtain at many native markets on the shores of Lake Victoria, the range is apparently wider and the flies exceptionally numerous, as was noticed and recorded by Dr. Wiggins, after he had examined many of these markets in Usoga. This is so, no doubt, because the food-supply is constant, plentiful, and easily obtained; and since the flies can follow inland for long distances in the shade, their opportunities for feeding are at a maximum. A like increase in numbers and in range would probably be found at habitual drinking-places of herds of cattle or game.

At any rate, I have noticed frequently that swarms of flies haunt the habitual shore-resorts of hippopotami and crocodiles; but here, strikingly enough, the range is not increased, for, in the case of water animals and those whose excursions on land are almost entirely at night, the opportunities for feeding would occur only at the water-side. In the case of man or land animals, however, where there is frequent or regular traffic to and from the water by day, the roads or tracks, and sometimes the bush generally, might become infested by "following" flies; for gorged flies, having fed at some distance inland, would often retire to the nearest shade to digest their meal, and might even feed again before returning to the water, but this would not occur to any great extent except in damp weather and where the scrub or some sort of shade was practically continuous for some distance inland from the water-side.

I think it highly probable that all flies encountered at a greater distance from water than about 80 yards are "following" flies; that is to say, they either are following or have followed persons or animals that have passed through their natural range. Where flies are exceptionally numerous and the conditions favourable, as in the wet season in a country thickly covered with scrub, and especially where there exists also, perhaps, a diffused condition of traffic, owing to the absence of open roads and a multiplicity of native paths through the bush, as was the case in South Usoga at the time of Dr. Wiggins's investigations there, it is quite possible that flies might be met with in such numbers as to make it appear that the long distances from water at which they are found constitute their natural range. And so, indeed, they do, to all intents and purposes, so long as such conditions are left untouched. But the point to which I wish to draw attention here is that wide ranges such as these can be abolished, just in the same manner and just as readily as the narrower ones, by dealing with the natural range alone. Take, for instance, a native market 300 yards from the lake shore, the canoe landing for which is in a fly area from which the shore fringe of jungle reaches inland for half a mile. The natural range from shore is probably really the average one of 10-30 yards, but, owing to the special conditions prevailing, many flies are met with, not only outside this, but also in and beyond the market itself. Clear the landing place and 100 yards beyond it on each side, along the foreshore to a width of, say, to be safe, twice the average natural range, which would amount to, at the most, 60 yards. Flies would then disappear not only from the cleared foreshore, but also from its hinterland of scrub, which includes the market, since they cannot remain away from water. Moreover, people coming to the market by canoe would no longer encounter flies at the landing and, therefore, they would no longer be constantly introducing them into the surrounding bush to replace those which had returned to the uncleared part of their natural range. So long as only the

cleared landing was used as an approach from the shore the market would, in fact, be now fly-free. The above clearing would be rendered more complete and perhaps safer by the addition of an open track, 20 to 30 yards wide, cut from the centre of the cleared foreshore to the market. Supposing that it were possible, instead of clearing the fly-infested landing, to close this and substitute a fly-free landing near by, the same results would ensue.

Dr. Wiggins's experiences in South Usoga were not only exceptional as regards the experience of the other observers, but were probably quite unusual in the locality itself. The seasonal conditions at the time were most abnormal with excessive rains, extensive floods, and an unprecedentedly high lake-level, so that he describes large areas as being covered with water, which was only hidden by the grass, and, in this flooded country, the fly was more or less scattered through the bush over a wide range from the lake, embracing practically the whole of small peninsulas such as Naniumba's, which is several miles across. On several occasions, too, he found these inland flies were more plentiful than at the corresponding lake-shore. This, perhaps, suggests the possibility of the fly having been actually driven inland from its natural haunts by the high lake-level and, since this has taken several months to subside, there may be reason to hope that some, at least, of the breeding-grounds along this shore have been destroyed and that, in the ensuing dry season, not only the range but the numbers of the fly may be found to have materially decreased.* The natives themselves said that the range had been increased by the heavy rains, and Dr. Wiggins was inclined to agree with them.

Apart from these abnormal conditions the fly is naturally more widely spread in this part of Usoga, owing to the indented character of the coast, the wide and thick jungle-fringe which borders it, and the numerous small streams which flow through this, many of which present patches of open water. The observations made here should be repeated under normal conditions in order to get a clear idea of the actual state of affairs.

It may be taken as a rule that the fly range is narrow where the forest or bush-fringe is narrow, but the reverse does not always hold good, since shade is not the only factor concerned. It shows, however, that the fly will not follow so far over clear or comparatively open spaces as through bush, forest, or high grass and other undergrowth.

It will be understood, from all that has been said, that the range, taken as a whole and including the "following" range, certainly varies much in different localities and under different conditions. I think it will be found to be practically sound,

* Not much is yet known as to the seasonal prevalence or variation of *G. palpalis*, but it is evident that a season of this kind would, by increasing its range, aid the spread of an epidemic.

however, in applying any general preventive measures, to take as a standard the average "natural" range and to adapt afterwards such a measure to local necessities.

I have mentioned that Dr. Wiggins discovered a small epidemic of sleeping sickness to the south-west of Mount Elgon. He describes it as being situated in the angle formed by the two rivers Marakisi and Rumba (or Chao), both of which enter the Mpologoma eventually, and between the Wehala and the Urororo (Tororo) Hills. This would place it, roughly, in a line between Mount Elgon and the mouth of the Sio River, about 20 miles north of Lake Victoria and about 10 miles from the mountain. The epidemic was said to be quite circumscribed and apparently completely isolated and to be, so to speak, burning itself out. It had commenced, according to local account, about five years previously, having been introduced from the people living to the west, many of whom were said to have died; and it was evident, from the already large mortality, that it had been of considerable duration. The name of the principal local chief, whose villages were examined, was Kapeto, and the rate of infection was still very high, being, in one village, estimated at about 80 per cent.

No connection could be traced between the fly-areas of this and of the Lake Victoria epidemic, though the epidemics themselves are undoubtedly related, and the smaller probably, though not certainly, of subsequent origin. Nearly all the streams flowing north from Usoga (also into the Mpologoma) on the one hand, and the Sio on the other, were found to be free from fly, but on the western or southern shore of the Mpologoma, some 30 miles to the west, at which part several of its Usoga tributaries enter it, some patches of fly were found and sleeping sickness was present. This small epidemic area seems to be situated in an outlying corner of the line forming the eastern limit of *Glossina palpalis*, which was very abundant there, the physical conditions everywhere favouring its presence. These are described as consisting of a series of scrub-covered hills intersected by streams overhung by dense forest. Many of the streams were in flood at the time of the investigation, and on the borders of several of these floods the fly was observed to be present.

Apparently this epidemic embraced the Warumbi, Wasetima, and part of the Wania, the first two small tribes having suffered very heavily; and the district reported on formed, probably, only the eastern end of it. There seems to be very little communication at the present time between the infected people and their neighbours, and, since there is no direct connection with other fly areas, there is little chance of the extension of sleeping sickness from this centre in either direction.

A word may also be said here about the Nile epidemic, since the conditions in that region and in part of Northern Unyoro differ from those existing in other parts of the Protectorate.

The main difference lies in the distribution of *Glossina palpalis*, owing to the open nature of the rivers and streams. Whereas in other parts the fly areas are for the most part confined to the outer boundaries of the province concerned, they are here dotted over the interior. That part of the Victoria Nile, indeed, which forms the boundary between Unyoro and the Nile Province, is certainly very thickly infested with fly, but the White Nile is haunted irregularly in larger or smaller patches (Note I.) and on long reaches of it, as, for instance, that between Wadelai and Nimule, these patches are both small and rarely met with, on account of the wide belts of sudd along the bank, while practically all the inland streams, wherever the conditions of shade, &c., are favourable, are dotted with fly-areas. These areas are usually small, the range from them is very narrow and the flies seldom numerous. Most of the villages are built outside the fly-range, and the only connection with the local fly-area is, in many, if not most, cases, through the water supply. I may mention here that the same condition holds in some villages on Lake Victoria, where there are others also in which almost the only connection is through the occupation of fishing and, nevertheless, in some of these villages the rate of infection is high, especially among the adult males. If the Nile natives were intelligent and amenable, this state of affairs might be dealt with comparatively easily by seeking fresh water-supplies or by clearing those which exist. They are, however, very backward and suspicious, and I see no hope of their taking any steps either to help themselves or to assist the Administration in protecting them.

The origin of the Nile epidemic does not appear to be quite certain and, although it was naturally supposed, when sleeping sickness was first discovered there, that it had spread from Lake Victoria via Lake Albert, there are, nevertheless, certain facts which are not in favour of this conclusion. Dr. Densham, who is investigating this epidemic, reports that very little information can be gathered from the natives generally, but that it seems to be agreed by most that the sickness first started, on this bank of the Nile, about four years ago at Ajei's, a chief settled on the Akkehr River between Wadelai and Nimule, while some state also that it was previously known to exist at a place Logwarri on the Congo side and was introduced from there. It is in favour of the alleged or even of a longer duration that the settlement at Ajei's referred to has been entirely wiped out by the disease and for so long abandoned that little or no trace of it remains, while the fact that not only have a large proportion of the cases so far examined by Dr. Densham originated in the Congo, but that a fair number of these have come from Logwarri* itself, seems to point to the probability

* Logwarri Lubari, on the Kibali, or Welle River, a tributary of the Congo River. See Map I. A centre of sleeping sickness is marked near here on the Liverpool Sleeping Sickness Commission's map.

of the alleged origin also. On the other hand, it is a fact that all the portage and a good deal of native trading, as far as our northern boundary and even into the Congo beyond, is done by enterprising natives of Uganda and Unyoro, and it is within my personal knowledge that infected Baganda and Banyoro have occasionally penetrated as far as Gondokoro within the last two years if not previously.

As I have pointed out above, under the conditions obtaining in this region, sleeping sickness would spread very slowly, and it would be a long time, after infection was first introduced, until it would be likely to have made considerable headway; moreover, it is a fact not to be ignored, in consideration of the origin, both of this and of the Uganda epidemic, that sleeping sickness might have been present among these people, who have come very little in contact with Europeans, for years without necessarily coming under observation, especially as their custom and instinct is to hide their sick; that it might even yet have remained undiscovered had it not been for special investigation, and might, possibly, have existed here even before infection found its way into Uganda.

In one other part of the Protectorate, namely, Ankole, the streams are mostly open but, since there is, as a rule, little or no shade on their banks, there is apparently no fly. The same will probably be found to apply in a great part of Kavirondo and in the country east and north-east of Lake Victoria. In western Toro, especially round Lake Albert Edward, fly are numerous in places and conditions exist favourable to an epidemic but, as I have already said, it has not yet been possible to make a thorough investigation. Steps are being taken, however, to limit the risks of infection being carried there from other epidemic areas if it should not have already arrived.

Although it is necessary to bear in mind certain hypotheses, it is well to remember that we probably can never know exactly how the infection of sleeping sickness reached East Central Africa. No doubt it came from the west, but the manner and route of its introduction we can scarcely hope to clear up with any certainty at this distance of time and with only native report to guide us. A more important question is whether, having once been introduced, it can ever be entirely eradicated, and it is to be feared that the balance of probability is against this. It is possible, of course, for there is no native evidence nor record of any value, no European knowledge extending over any lengthened period, that sleeping sickness had visited these regions in former times and that the epidemic had been rolling slowly to and fro from the west coast to the great lakes at intervals, perhaps, of centuries, leaving in its track endemic centres scattered here and there across the continent. It is more probable, however, that the present epidemic is the result of the first introduction of infection and that, once introduced, it will remain endemic in certain areas specially favourable to it, such as, for instance, parts of Usoga. Whatever the truth

as to this may be, it is certain, that, wherever *Glossina palpalis* exists, we must expect epidemic outbreaks to be more frequent than in the past, owing to the increased frequency and facility of inter-communication. Many facts, too, such as the nature of the disease itself and of the infection causing it, of the carrier, its haunts, and its local numerical prevalence, render it difficult to suppose that it can be utterly abolished, in certain localities especially suitable to the fly, any more than can malaria, and it is, therefore, probable that it will remain endemic in a few parts of the Uganda Protectorate.

Perhaps there is just a possibility that *Glossina palpalis* may have its cycles of great increase or decrease, becoming, during the former, far more numerous and widely spread than at other times, while the latter may be of sufficient duration to allow the infection to die out in the vertebrate hosts in those localities from which it would for the time disappear. At least, I believe that there are certain lepidoptera, such as the clouded yellow butterfly, which, though ordinarily strictly localised, in certain rare and favourable years, spread in large numbers over regions from which they have been long absent and again, eventually, disappear from them as completely as before and become confined to their former limits. The close connection of *Glossina palpalis* with the waterside might seem to offer some prospect that its local prevalence might be largely influenced by abnormal rainfall or drought. Apart from speculation, however, seeing that there is a probability that sleeping sickness will remain endemic with us, it behoves us the more to consider some means whereby its ravages may be so far checked that it may cease to be a bug-bear to the people and a barrier to the development of the country.

Perhaps the most striking fact in connection with the distribution of *Glossina palpalis* and the spread of sleeping sickness is the enormous amount of traffic which is shown to have existed and to exist still, though in less degree, between the whole extent of the shores of Lake Victoria and the natives of from 10 to 20 or even 30 miles and more of the hinterland. The fact is apparent when we consider the extreme narrowness of the average fly-range, the few instances (scarcely any, except in South Usoga) in which the fly penetrates inland along the streams, and the distance (not very wide but vast as compared with the few hundred yards of fly-range) to which the epidemic has spread from the lake. The percentage of the infection varies, as one would expect, with the distance from the fly-ranges, and is most marked within the first four or five miles, sometimes considerable within 10, while, beyond this, it is much less, though quite noticeable in places.

We find a decidedly high percentage in many villages which are situated near the lake but outside the fly-range, and this decreases with the distance from the lake and inversely as the amount of traffic therewith, supposing the traffic to be with the infective areas. Some villages situated just outside the

local-fly-range (which generally means that their water-supply happens to be free) show a high rate of infection because the occupation of practically all their inhabitants is fishing. Many others are connected with the fly-range only through their water-supply, and some through the occupation of canoeing.

It is clear, then, that before all things these two conditions, the width of the fly-ranges and the traffic with the fly-ranges, must be considered in dealing with the spread of infection, and full consideration is, therefore, given to them in the suggestions and recommendations put forward in this report.

For example, water-supplies or dipping-places and also canoe-landings can often be rendered safe by clearing, and this, therefore, can be recommended where it is necessary and practicable; or they can be closed and, in certain instances, safe ones substituted. In the case of fishing, however, unless in a few more favoured localities, nothing practical that we can do can make this safe as an occupation, so that I recommend later on its total discouragement or disuse, except in special areas or cases in which it may be found possible to regulate it satisfactorily, and this more especially since a great part of the trade and traffic with the lake shore is connected with fish.

It appears to me that, so far as we have gone at present in our studies of sleeping sickness in the human subject and inoculated animals, and of *Glossina palpalis*, its habits and distribution, all things combine to indicate the importance, whatever may be the outcome of the arduous search for an organic or medicinal cure, of the study of prevention and of the necessity for directing our immediate endeavours towards determining, by adequate trial and experiment, what general preventive measures may be practicable in the countries and under the conditions where the disease exists, and, further, that we should seriously consider the advisability of applying, without further delay and to the best of our knowledge, such measures as appear to give the greatest chance of success. For, even if a cure be ultimately found, it is extremely unlikely to be of such general efficacy and applicability as to render preventive measures of less than the first importance in controlling the spread of the infection, since it must be remembered that it has been by such means, and not by medicinal cures, that the greatest and most permanent success has been achieved in the past in combating other deadly epidemic diseases such as plague, cholera, typhus, and enteric fever, and that none of these diseases has been overcome, as it were, in pitched battle, but in each case by continued effort and the gradual diminution of its power of attack, the success at present obtained being probably, in most cases, far beyond the hope or imagination of those who began the contest.

If, after reviewing all the facts, it should be decided that the probability is against the success of general preventive

measures, or that their application would be impossible, then it would be better at once to cease spending time and money in this direction beyond what is necessary for the protection of certain limited areas, such as European stations, &c., and to await in patience the discovery of an undoubted and effectual cure.

It is my firm belief, however, that the present position as regards prevention, though beset with difficulties, is very far from being hopeless, and that the measures herein recommended would eventually be rewarded with a valuable proportion of success in the Uganda Protectorate, though it may be some considerable time before they can be fully applied and before they can produce any very marked effects.

Every one knows that we cannot, in the nature of things, hope to cut short a great epidemic of sleeping sickness with the promptness with which we might check an outbreak of an acute and rapid disease like small-pox or plague, but I believe that, nevertheless, we ought to set out on the same lines at once and on all hands to try, by all practical means in our power, to diminish the chances of infection just as we do in the case of all other infectious diseases.

No doubt certain preventive measures most valuable in other epidemics, such as isolation of the sick, quarantine and cordons, have, owing to the peculiar characteristics of sleeping sickness, been evidently from the first impracticable of anything like general application. Yet, if the bulk of the population with which we have to deal were Europeans, the task of prevention would be comparatively easy, and I believe that our main difficulty will lie, not so much in the great differences of sleeping sickness from other epidemic diseases, as in the peculiarities, prejudices, and, worst of all, unreasoning apathy of the peoples whom it attacks and the conditions in which many of them are accustomed to live, so that our main duty, therefore, is to determine what measures there are which may remain open to us for diminishing the risks of infection, and what prospects of success we may hope for in applying these among such people.

As has before been mentioned, the Sleeping Sickness Extended Investigations have everywhere tended to strengthen the association of epidemic sleeping sickness with the presence of *Glossina palpalis* and even, to that extent, to indicate it as the sole carrier of *Trypanosoma gambiense*. The infection, though carried from person to person by the fly, is, as a general rule, conveyed from place to place by man, so that the process of its spread must be regarded from these two aspects. So also its transmission between vertebrate hosts, being indirect by means of the invertebrate, must be considered from two points of view:—

- (1) Infection of human beings by infected flies.
- (2) Infection of flies by infected persons.

The fly, if kept from contact with infected persons, is harmless, and the infected person, if kept from contact with the fly, is also harmless.

How, then, can we limit the natural possibilities of infection in each case? Broadly speaking, our objects can be attained:—

- (A) By diminishing the chances of exposure of human beings to the fly, especially of the sick, *i.e.*, by diminishing the opportunities of the fly for biting them.
- (B) By exterminating or reducing in numbers the fly,* especially in places of human concourse or traffic.
- (C) By diminishing the chances of infection being carried by infected persons to or from epidemic or potential epidemic areas.

The chief measures to be discussed or recommended in relation to these various objects will interact to a great extent, but those which are more special to each are as follows:—

- A.—(1) Local segregation of the sick (Note I.), including deportation and with or without local concentration.
- (2) Removal of huts, villages, markets, &c., from within the local fly-range.
- (3) Protection of the person by clothing (including education of natives to resist and avoid the bite of the fly).
- (4) Regulation or selection of hours for certain occupations within the fly-range.
- (5) Protection of employees exposed in their occupation to the attacks of the fly.
- B.—(1) Directly by killing or catching the flies.
- (2) Possibly by introducing some destructive animal, morbidic or parasitic agent among the flies.
- (3) Indirectly by destroying their haunts and breeding-grounds, *i.e.*, by clearing jungle and undergrowth, especially in the various fly-areas connected with places of human concourse or traffic.
- (4) Possibly by destroying or diminishing their food supply.
- C.—(1) Control or surveillance of travellers, traders, and emigrants from epidemic areas, and especially of their settlement or residence in or in contact with non-infected fly-ranges or potential epidemic areas.
- (2) Regulation and surveillance of camping places, transport-stations, &c., on traffic-routes by land and water, including effective clearing or diversion where these come in contact with fly-ranges.

* Including, of course, the larvæ or pupæ, should this become practicable.

Before discussing the above I may perhaps mention that I have from the first been struck with the important bearing on preventive measures of the fact or accident of the relative immunity from sleeping sickness of Europeans and of certain of the better class of natives, and by the necessity for ascertaining on what conditions this immunity depends and how the protection which they afford can be extended, to any useful degree, to the ordinary native. It soon became evident that this apparent immunity depends on one main governing condition only, viz., exposure to the bite of *Glossina palpalis*, and on certain subsidiary ones such as clothing, customs, habits, occupations, dwellings, and especially the situation of dwellings, which determine the amount of such exposure.

I, therefore, drew attention, in May, 1904,* to this relative immunity of Europeans as pointing the direction in which was to be discerned the greatest hope for the native, and recommended, in connection with it, the systematic clearing of the usual places of human resort in infected areas and the removal of the sick to open spaces beyond the fly-range, as measures which would greatly diminish the risk of infection run by the majority of natives, especially the women and children, and would lessen the probability of the future occurrence of widespread epidemics.

After further investigations (Note 1) which showed, what I had already hoped might be the case, that the range of the fly from water was far narrower than had previously been supposed, at least in the region then examined and at the season in which the observations were made (these observations also pointing to the probability that the breeding-grounds were always very close to the waterside), I again put forward the above measures as being the most practical and the most likely to produce satisfactory results, laying special stress on the importance and apparent feasibility by the natives themselves of "local segregation" of their sick beyond the bounds of the neighbouring fly-ranges.

I have now, after comparing the observations then made with the reports received in the course of the present investigations, come to the conclusion that some such measures as these are not only the most important which can be undertaken at the moment but that the time has arrived when their general application should be begun, since, as I have already stated, our knowledge is now sufficient for their practical use, and they seem, besides, not only to decrease in magnitude and difficulty with further investigation, but also to give, at the same time, greater hope of beneficial results. Moreover, I am convinced, for my own part, that the natives, if they were willing and would be guided, could apply both these measures, locally, to a

* Islington Medical Society, May 17th, 1904; "Lancet," July 30th, 1904.

sufficient extent to check the present epidemic, and to avoid future outbreaks of any magnitude without any great hardship or expense. I fear, however, that this will remain a possibility only, since their attitude is that of the negro generally, and they seem to expect to be paid by Government for any labour which they are recommended to undertake to save themselves from extermination. In some parts, especially in the Uganda Kingdom, the more intelligent will in time, perhaps very soon, appreciate the value of the advice that is now being given them, but it is doubtful if, even then, they will be inclined to carry it out for any useful period except under strong pressure.

Clearing and segregation, then, I place first of all the measures enumerated above, and the former, because it has already been applied locally and its utility proved; and because it also has an important bearing on many of the others, I will discuss it first in detail.

No doubt this measure would occur, as an obvious method of extermination of *Glossina palpalis*, to anyone who has been engaged in the study of sleeping sickness or has been especially interested in its prevention, but it is only of late that it has appeared to be either possible or worth while as a more or less general measure. In order to apply it scientifically there is no doubt that much remains to be done by experiment and research to enable us to combine the amount and method which shall be at once the most effective and the most economical; but I hope to show, nevertheless, that it should be applied as generally and as speedily as possible to all places in or in contact with infective areas the use of which is necessary for human resort, concourse or traffic.

At first the clearing of the forests and jungles for the purpose of exterminating *Glossina palpalis*, or even of appreciably diminishing its numbers, seemed a task too gigantic to be considered, except for a few special circumscribed localities. It was supposed that the whole of the vast forest and jungle-covered areas of the country, and even the immense swamps, might have to be dealt with in order to insure success. Further investigation has shown, however, that the haunts of *Glossina palpalis*, or fly-areas, are narrow and circumscribed, and their situations localised strictly by certain physical conditions; that their natural range from the waterside is limited, and probably never exceeds 50 yards, and that this, in the scientific application of clearing, is practically the only distance that need be considered, since the wider "following" range, which itself amounts to only a few hundred yards on the average, may almost be neglected.

More than this, it is extremely probable, though its larvæ have not yet been discovered* in natural conditions, that the

* See Appendix (B). Discovery by Dr. Bagshawe since the above was written.

breeding-places of *Glossina palpalis* are always close to the water's edge, and that a very narrow strip of clearing would suffice to destroy them as breeding-places.

No doubt the general distribution of *Glossina palpalis* is governed by the presence or absence of suitable breeding-grounds, and its local range and numerical prevalence by the physical and climatic conditions prevailing at the breeding-grounds and by the opportunities for feeding. That these breeding-places must be very near to water seems practically certain, because the presence of the fly at any given spot is determined, chiefly at all events, not by the general facts of climate, but by the extremely local physical conditions which exist at the very margin of the water where it is found. It would even seem that the necessary conditions may vary more widely on the water than on the land side of the line of the water's edge. Hence it may prove that the strip of clearing which will be necessary on fly-infested banks and shores may be even narrower than the average fly-range, and it will have to be undertaken only on "open" rivers and on shores free from wide swamp-belts (where, in fact, there is a certain amount of open water with contiguous shade, and with, in places, more or less defined bands for breeding-grounds), and may be limited chiefly to places of human concourse, where the fly is most liable to become infected. Moreover, as soon as we can recognize their limits, with sufficient accuracy, it will probably be sufficient to attack the fly only or chiefly by destroying the breeding-places with their pupæ.

But, even when the extent or distance of the breeding-grounds from water is accurately known, as it is hoped will be the case ere long, the exact width of clearing necessary on the average (for it is practically certain to vary somewhat in different localities) can only be determined by careful experiment.

Although vertebrates of various kinds have been artificially inoculated with *Trypanosoma gambiense*, yet, so far as is known at present, there is no wild or domestic animal which, itself almost or quite immune, carries this *Trypanosoma* so habitually as to act as a "reservoir" for the infection of sleeping sickness, as do the big game in the case of the *Trypanosoma Brucei* of Nagana. No animal, indeed, except the native dog,* and that in only a few instances, in places where the degree of local infection has been intense and the epidemic has been of considerable duration, has been found to be naturally infected; on this point, however, further research is much needed, for, if there be such a reservoir, it is most likely a domestic animal, and might possibly be the native dog itself; at any rate it is unlikely to be an animal which ranges, and

* *Vide* Appendix C. Professor Koch informs me that in the Sese Islands one monkey has been found, by one of his staff, to be naturally infected.

would therefore carry the infection, very widely. It is obvious that animals which can become naturally infected by *Glossina palpalis*, unless the fact is very exceptional, are an added danger to the community.

Meantime we must provisionally suppose that only the human being and the fly need be seriously considered as agents in the spread of infection, that the vast majority of flies, where human being are scanty or absent, are uninfected and harmless in themselves, and that, if fly could be eliminated from places of human concourse such as mentioned above, those existing elsewhere would run little chance of becoming infected.

It is probable that only a small percentage of flies in an infected area (taking it as a whole) carry infection, though there may be certain very limited localities where the percentage may be, at times, comparatively much higher. The average percentage of human infection also is very hard to determine with any exactness, because of the difficulty, except by such comparatively tedious, and, to many natives, terrifying measures as gland-puncture, of obtaining as a standard an even approximately true percentage in any given district or fly-area. The palpation of glands, in such places as Uganda and Usoga, where such diseases as itch or craw-craw and syphilis are very common, is apt to be very misleading.* But, unless the average percentage of infected flies were low, it is difficult to understand how, in certain highly-infected localities where for months and months every native has been daily exposed, along with sick people, to swarms of flies, any single soul has escaped alive. Many Europeans, too, both before and since *Glossina palpalis* became known as the carrier of the infection of sleeping sickness, have been bitten by it and yet have so far escaped the disease, and in this there is some analogy with the relation of the bites of *Anopheles* to infection with malaria. In the case of spirillum fever, on the other hand, where infection is hereditary in the invertebrate, and a large proportion of the ticks on certain roads and in certain districts is infected, practically all Europeans who expose themselves to their bites contract the fever. It seems fairly certain, also, that those trypanosomes which have been found, in certain tested localities, to exist in from 0.5 to 8 per cent. of the flies examined, are not the *Trypanosoma gambiense* and do not cause disease when inoculated into susceptible animals, so that even these small percentages may be too large in the case of *T. gambiense*. The flies are forest or jungle insects, not in any sense "domestic," and the great bulk of them will always exist in places where human beings are scanty or absent and infection is rare. Thus the risks are practically confined to

* It is but a rough test in the hands of experts. As a guide for persons unacquainted with the characteristic glands of trypanomiasis it is quite untrustworthy: moreover, glandular swelling is not invariably perceptible in every case.

places of human concourse, to which, therefore, the preventive measures of clearing can be chiefly limited. It is important, however, that these clearings should be carried out not only in infected but also in non-infected fly-areas.

In spite of all the time and labour that has been expended in anatomical and bacteriological study in connection with *Glossina palpalis*, *Trypanosoma gambiense* and sleeping sickness, and in spite of all the expert skill which has been engaged in this task, we do not yet know, so far as I am aware (for I have not at present seen the account of the last stage of the work of the Royal Society's Commission in Uganda nor any very recent publication dealing with the subject), whether the trypanosome undergoes a cycle of development in the fly, nor, if so, at what stage or stages of its evolution the bite of the latter is infectious, nor, in any case, for how long a fly carrying trypanosome may remain infectious, nor do we know even the average duration of the fly's life in natural conditions, supposing that it is capable of life-long infection.

This being so, we cannot, in applying preventive measures, however sure we may feel of an ultimate proportion of success, obtain any clear idea either of how soon we may expect diminution in the infectivity of depopulated infective areas, nor within what time we may relax our precautions, nor can we gauge even the approximate risks of infection in such areas. It is evident that the shorter the period of infection in the fly, the less chance there is of it infecting by its bite after once acquiring the infection, and the less will be the number of persons whom it is likely to infect, since, as a rule, it naturally feeds only once in 48 hours; and the converse of course is also true. Analogy with other protozoal organic infections points to the probability of a cycle of development in the fly, of a non-infective period of evolution preceding the infective stage, and of a long, if not life-long, infectiveness of the invertebrate host. But all this, in the present imperfect state of our knowledge of trypanosomes and of trypanosomiasis, remains nothing more than suspicion.

The facts which I have adduced, for they can scarcely be called arguments, in favour of a low percentage of infection among the flies of a given area are, so far as they go, also in favour of the limited duration of infection in the fly. In addition, also, I will relate the case of a small settlement of seven huts which I came upon in Usoga some four years ago. These huts were situated on the point of a small and narrow peninsula of a few acres in extent, the whole of the point for 60 or 70 yards being covered with jungle, which practically surrounded the little settlement, while, beyond this, the base or neck of the peninsula was formed of 100 yards or so of low swampy ground extending landwards between wide areas of papyrus. The point itself swarmed with fly as far as the jungle extended, but, on the swampy ground beyond, there were few

or none. The inhabitants were 19, of whom all but five children, two women and one man had sleeping sickness, and these people (for no one else lived anywhere near), with four or five goats and a few fowls and perhaps an occasional hippopotamus and some wild birds, must have formed the whole available source of food for the flies on this small area. I was not able to follow the history of these people, for the peninsula was soon afterwards deserted, but of my 14 canoemen I knew the history of eight for the next six months, and only one of them happened to develop sleeping sickness, though probably they had undergone many other exposures to infection. Of three servants who were with me none has any sign of sleeping sickness to this day, nor have I myself, though not one of us could avoid being bitten by the swarming and persistent flies at that stricken spot. One would suppose that there would be hardly a fly there that had not many times bitten one or more of the eleven inhabitants who were certainly infected, most of whom were lying about freely exposed to their attacks at the time of my visit, and it appears to me that, if the infection in the fly were lifelong, or even of considerable duration, most or all of us who were bitten then should have become infected, and I cannot help but think, in consequence, that there is some ground for hope that the period of infection in the fly is either of very short duration or is made up of very brief intermittent stages. It is even possible, still, that the conveyance of the infection by *Glossina palpalis*, rather than by other *Glossinæ*, or by any blood-sucking insect, may be merely owing to a prolonged viability of the trypanosome in the interior of this fly, that a migration rather than an evolution takes place, and that it is not a true host.*

I understood from Captain A. C. H. Gray, R.A.M.C., that the trypanosomes which one finds swarming in the intestine of a varying small percentage of *Glossina palpalis* were found by Tulloch and himself to be non-pathogenic to animals susceptible of infection by *Trypanosoma gambiense*. There is doubtless more than one type of these trypanosomes, besides individuals resembling *T. gambiense*, but, so far as I can ascertain, no one has yet certainly demonstrated the presence of this trypanosome in *Glossina palpalis* after all the blood of a meal has disappeared by complete digestion.

In my opinion the questions of the duration of infection in the fly and of the capacity of other species of *Glossinæ* than *palpalis* of carrying the infection are the most important and most urgent for investigation at the present moment.

That wholesale clearing of the foreshore and for some distance inland will effectually eliminate *Glossina palpalis*, so

* I have since read the "Preliminary Report on *G. palpalis* in its Relation to *T. gambiense*, &c.," Minchin, Gray and Tulloch. It appears that their conclusions from direct experiment point, like deductions from general observations, to a short period of infectivity in the fly.

long as the clearing is maintained on the foreshore, has been conclusively proved at Entebbe, where, for the last five months, from March 31st-August 31st, 1906, it has been impossible to obtain a specimen from places in which it lately swarmed, whilst, immediately beyond the limit of clearing, it remains as numerous on the foreshore as ever.

The following experiment, which is now in progress, will, I hope, lead to definite results of scientific and economic value on this point. I propose that the extended clearing of the foreshore of Entebbe Bay, which had already been recommended as highly necessary, shall be carried out thus:—

A strip of 200 yards in length having been cleared along the water's edge to a width of 30 yards, the results as affecting the fly will be carefully watched, and, if necessary, the width will be increased by strips of from five to ten yards until the fly disappears. If the width of 30 yards proves sufficient, the next strip of 200 yards along the foreshore will be cleared to a width of 25 yards only, and the result watched as before, and so on with fresh strips till a definite knowledge is obtained of the width to which successful clearing should be carried. The lake shore here is readily accessible for frequent observation and supervision, and, since it is fairly thickly infested with fly and very densely covered with a moderately wide belt of forest and undergrowth, the test should give a reliable average for most foreshores.

It is probable that a still larger experiment, embracing the whole of the Entebbe Peninsula, will also be undertaken.

A line would be drawn from the head of Kesubi Bay to the head of the opposite bay on the western side, and the whole peninsula south of this would be dealt with by the clearing of inhabited and fly-infested foreshores, ferries, landings, watering-places and native markets, and by the removal, where necessary, of natives and their dwellings from the fly-range, so as to form, if successful in any marked degree, an object lesson to teach the natives what they can do for themselves; and I have great hope that this will be both practicable and ultimately successful. Most of the statistics of this peninsula necessary for the experiment have already been obtained with this object in view, but they will have to be corrected by further observations unless a beginning of operations is soon made.

I believe the above-mentioned area to be the most favourable which can be taken, for the following reasons:—

- (1) The fact that it is a peninsula, is accessible, and can comparatively easily be overlooked by the Administrative and Medical Authorities.
- (2) That Entebbe might naturally be looked to by the natives as the centre of our endeavours against sleeping sickness.

- (3) That this area is well known to the natives to be in many parts thickly infested by fly, has had a bad name among them for sleeping sickness in the past, and is certainly not a locality of which they could afterwards say that what has been done here cannot be done in most other places.

It is necessary to bear in mind, however, in this or any similar experiment, that, even under the most favourable circumstances, it will be impossible to stamp out sleeping sickness suddenly and at once. Success will have to be measured by the decrease in fresh cases in proportion to the existing population, but, for some considerable time, a great though diminishing fallacy will be present in the fact that a certain number of the inhabitants are doubtless already infected, and, owing to the incubation or febrile period being sometimes prolonged to several years, many *new cases* may be cropping up during that period, although there may have been very few or no *recent infections*.

It may be found possible, however, by systematic examination of glands and by means of gland puncture, to get a fairly clear idea of how many of the cases are due to former and how many to recent infection.

In addition to these experiments certain areas such as the foreshores at ferries, fords, canoe-landings, village dipping-places and native markets, have been specially recommended for clearing; and this is being done, where possible, either wholly or partially by the natives themselves. Such places are being noted monthly in their reports by the Medical Officers of the Sleeping Sickness Extended Investigations, who are directed to instruct the local chiefs as to the connection of *Glossina palpalis* with sleeping sickness, the reasons for clearing, the situations where it is necessary and the amount which will probably be required. These instructions are being supported by the Administrative Authorities, and in due course the Medical Officers will re-examine these clearings and note their local effects as regards the fly, the use the natives make of them and whether they are keeping them in effective order by planting or by other means.

I have proposed also a more general scheme of clearing for serious consideration, namely, that the cutting of fuel on the mainland and islands for steamers and other purposes should be restricted as much as possible to such localities as, now and hereafter, may be recommended for especial clearing and, outside these areas, to a zone not more than a hundred yards in breadth from the water's edge. I have also suggested that the cutting of timber, for any purpose for which it may be required, might be encouraged within the same limits, provided that the undergrowth is also removed, the regulations on this head to be applied to the great lakes and to such rivers as are used for navigation, wherever *Glossina palpalis* is present on the margins.

The undergrowth, when cut, should be collected and burned along the waterside, so as to aid in the destruction of any pupæ which might be deposited there.

It is hoped that means may be devised of storing and stacking the green wood for drying at convenient places, so that the wood-cutting necessary for the large and increasing amount of fuel consumed by the steamers may be turned to account for the special clearing required, and the value of the fuel set off against the expense of the same.

To revert to special clearings at places of human concourse, it is probable that none of these need extend over more than a relatively small area, and that, in the case of fords, ferries, landings and dipping-places, a strip of bank or foreshore 200 to 300 yards long and perhaps not more than 50 to 100 yards back, with a wide track from it, where the fringe of forest or jungle is deeper than the width of the clearing, to the nearest road, market or settlement, will in most instances suffice. In making these clearings for natives it will be well to remember that a few tall shade-trees, well isolated, and as nearly as may be in the centre of the cleared space, should, wherever possible, be left standing, or, failing these, an artificial shelter built, for otherwise many natives will not use the clearings at all, but will sit, eat and sleep in the jungle at their margins.

Wherever clearing is undertaken in order to banish the fly it will be necessary to keep open the cleared spaces, and, at the same time, to avoid the endless labour and expense inseparable from the constant re-cutting which would be required to keep down the undergrowth in a climate in which it renews itself so rapidly as in the Uganda Protectorate, and the only way to do this effectually seems to be by planting some grass or small plant which by its hardihood will retain a hold on the ground while affording no efficient shelter for the fly. Of course the best, economically speaking, would be such as would give some marketable return, if such can be found. His Excellency the Commissioner has instituted at Entebbe the planting of citronella grass, and this has hitherto been perfectly successful as regards the fly. Probably the best substitute for it in many native clearings will be either the sweet potato, the ground-nut or sem-sem, according to the nature of the soil. Bananas afford too much shade for it to be safe to plant them close to the waterside, though a shadeless space of 30 yards or so between them and the water seems to be sufficient to keep the fly out of them.

It will be safer and cheaper, in the case of huts and villages wholly or partially within the fly-range, if they cannot be removed altogether, to move back the dwellings out of range and to make a clearing such as has been described above to connect them with the water supply. The distance which they may need to be moved in order to be beyond the fly-range may possibly vary from 50 yards to half a mile, but, in some cases,

as where they are situated on a very narrow bush-clad peninsula difficult to clear, or where the fly-range is abnormally wide, it would be imperative to remove them altogether. It will seldom, in fact, be wise or necessary to clear whole settlements within the fly-range. If they are far enough back and sufficiently well situated, the foreshore, with a communication from it to the settlement, may be cleared, otherwise they should be removed. Where the inhabitants are very few or the sick are very many and communities are therefore unable to take the ordinary precautions, or where they are refractory and refuse to do so, they should be deported to some fly-free area in the interior.

What has been said of huts and villages applies in most instances to native markets. Some of them may have to be entirely cleared, some moved further inland and some abolished. These markets are notoriously situated in the very worst places as regards fly, and have probably, as has been suggested above, actually caused the superabundance of flies that infest them. No attempt is made by the natives on their own account to clear them; they are widely resorted to by both sick and sound and by both coast and inland people, as well as, in many cases, by islanders, and are probably the most dangerous centres of infection which exist.

I am strongly of opinion that, where natives refuse or are unable to undertake the necessary local clearing, they should, for the sake of the community, be forbidden to occupy villages or to visit markets within the fly-range, wherever there is a reasonable chance of enforcing their obedience; and that, where there is little or no chance that natives, either on account of the natural difficulties or of their own indisposition, will deal effectively with their own settlements, they should be deported inland to a fly-free area at such a distance as will make communication with, or return to, the fly-range difficult. For while, theoretically, persons and villages need usually be removed only a few hundred yards in order to be, with proper care, safe from fly, yet, as a matter of policy and administration, in dealing with African natives, there will be no safety except at a much greater distance, at which moreover it is possible that some form of concentration may be feasible, and this, as His Excellency the Commissioner has pointed out, would be a great advantage in the application of any form of successful treatment which may be discovered; it would, moreover, be favourable for purposes of supervision, and for keeping statistical records. Any form of concentration near the lake shore or within easy distance of fly-ranges I consider in the highest degree inadmissible.

The protection of the native employees engaged in occupations such as rubber collecting, which may in some places expose them to the attacks of the fly, is also mainly a question of clearing, and would be met by inserting provisions in leases and concessions which would insure the clearing by the em-

ployers of such landings, camps, collecting and storing stations, &c., as are situated in the fly-range. Native labourers should also be encouraged to wear a more efficient covering in the way of clothes as a protection against the fly, but this would be of very little use to them until they have learned to avoid or resist its bite, which they are only just beginning in a few places to regard at all. It is still common enough, where the fly is plentiful, to see half a dozen or more flies feeding quietly and unnoticed on the nude body of a native.

The dangerous occupation of fishing should be discouraged as much as possible and should be forbidden altogether in those localities in which it is impossible to restrict it within fly-free areas, or where no such areas exist of sufficient extent to allow of its proper regulation. Certain villages, as I have mentioned, are only or mainly in contact with *Glossina palpalis* through this occupation, while the fish trade is the chief, or one of the chief, causes of the traffic of the hinterland villages with the lake shores.

I fear that little can be done with reference to the regulation or selection of hours of occupation within the fly-range, since there is no absolute safe margin of time either in the morning or the evening during daylight. Some use may be made, however, of the fact that *Glossina palpalis* is much less active before 8 a.m. and after 4.30 p.m., especially by villagers for such purposes as bathing, drawing water or washing clothes, and by travellers for camping and breaking camp; and also, for some purposes, advantage might be taken of the fact that they are almost entirely inactive in wind and rain.

The term "local segregation" of the sick I have already used and briefly explained above. It consists in the removal of the sick of each hut, village or settlement from contact with the local fly-range, prohibiting them from visiting the waterside and supplying them with water and also, where necessary, with food as well. I showed in my above-quoted report (Report VIII.) that this could easily and with little or no expense or hardship be carried out by each village or chief separately, because, so far as the fly is concerned, the removal of huts and of patients need be, in very many cases, only from the waterside to the next hill or open space behind the forest fringe, often only a few hundred yards. I fear, however, that, in most parts of the Protectorate, the natives could not be trusted to carry out even these simple measures sufficiently strictly or for a sufficient length of time to produce satisfactory results. I am confident, however, that in some parts, where the natives are more intelligent and more under European control, as in the Uganda Kingdom and possibly Usoga, the advantages of these measures will be eventually understood and that a fair number of villages would undertake them if supported by their chiefs. Any general application of segregation to the Protectorate as a whole would, however, have to be undertaken by Government.

The plan is very simple in itself, and I consider it of equal if not of greater importance than clearing both in its suitability for general application and as a preventive measure, and that every effort should be made and every assistance requested from all classes of Europeans and from the higher and more intelligent chiefs, to induce the natives to acquiesce in it, even where they do not take it up actively themselves. For, even if it were only partially carried out, it would enormously diminish the risks for many people, and also the chances of infection and constant re-infection of large numbers of flies, and would tend to increase the safety not only of the villages wherever it is adopted, but also of travellers passing through. The less the natives undertake it, however, *i.e.*, the less "local" it can be made, and the more the Government are obliged to take it in hand, the more concentration will be required and the more it will probably cost to carry out.

There is, of course, the difficulty of detecting the disease in its early stages, but, on the other hand, it is the advanced and easily recognised cases that, lying about torpid near the water-side, present by far the greatest opportunities to the fly. Further, the detection of early cases is much easier to the natives themselves, since they are able to note, in their relations and acquaintances who are under their constant observation, those changes of mental attitude or habit and the intermittent symptoms which occur so very early in the disease, with far more certainty than can a medical man in isolated examinations. The more heartily, therefore, the natives can be persuaded to enter into any such scheme, the more completely will infectious cases be removed from infective areas.

This measure, in fact, in common with others of any magnitude, has the disadvantage that, even if it be undertaken and supervised by Government, it cannot be thoroughly carried out without the co-operation of the natives, and, since it is so important in all preventive measures which may be attempted, including the enforcement of precaution on individuals for the sake of the community, that native co-operation should be obtained, I have compiled an address to natives on the subject of sleeping sickness, the fly, and the measures of clearing and of segregation, in which I have tried to explain the present situation as simply as possible. I propose to get this address translated into the languages of the more intelligent natives, and afterwards printed and circulated wherever there is a chance of its being read and understood. (It is already being circulated in Luganda. Appendix D.). A copy has already been submitted for approval, and one will be found attached to this report. The importance which I attach to native co-operation or, at least, acquiescence, is manifest in the address itself.

Where the villagers are unable or disinclined to segregate their sick and to take the other precautions recommended to

them, which I fear will be the case in most places outside the Uganda Kingdom and in not a few within it, I am of opinion that measures should be taken to deport them to such parts of the interior of the Protectorate as are free from fly and, since our investigations show that fly-free country is available in each county and district affected by sleeping sickness, there need be no question of removing them far from their friends or native soil, for a centre might be found in each chieftainship, county or district for segregation of the sick and for deporting, from within the fly-range, those who are refractory or so apathetic as to be a danger to others.

The removal of huts and villages from contact with the fly range has already been alluded to in connection with clearing. The Medical Officers of the Sleeping Sickness Extended Investigations are investigating this range and, as soon as it is determined in any place, the removals should be carried out without delay. In Uganda and other places where the chiefs are intelligent it should, theoretically, present little difficulty, yet unless the removal is to the interior, it must be accompanied in most cases by clearing the fore-shore and a way to the water-supply, and the natives can seldom be depended on, without periodical inspection, to keep up this clearing over any prolonged period. In many parts, especially the Nile and parts of Unyoro, where they are backward and full of suspicion, they cannot be depended on to do anything at all for themselves, so that removal to safe localities is the only course remaining open, and should be carried out where possible. The conditions in the Nile Province do not point, as I have already stated, to the likelihood of the occurrence of a very great epidemic, such as that on the Victoria Nyanza, though the eventual loss of life will probably be large as the disease smoulders, perhaps for years, among the scattered villages. Not the least obstacle to the general application there of any measure lies in the frequent and indiscriminate and probably as yet uncontrollable crossing and recrossing of the river by considerable numbers of the natives to and from the Nile Province and the Congo Free State. It is quite possible, indeed, that by this channel the infection first found its way into the Uganda Protectorate, as I have hinted elsewhere, in speaking of the Medical Officer's reports.

The experiment of reducing the number of flies locally by capture has been tried incidentally at Entebbe. Here flies were captured for scientific purposes by from two to six fly-boys, who brought in on an average perhaps 100 to 150 each per day, almost daily, for several years. These boys went almost always to a certain part of the fore-shore where flies are plentiful, and I was able to examine this fore-shore both soon after the captures commenced and also a short time before it was recently cleared of undergrowth, when I could perceive no difference in the number of flies, which were still very plentiful. After the clearing, however, the boys had to change their

hunting-grounds to an uncleared part further up the bay in order to obtain specimens.

With regard to the possibility of introducing some destructive animal agency, disease or parasite among the flies, I am not aware that any experiments have yet been attempted in this direction.

As to the possibility of reducing the number of flies locally by limiting their food-supply, this is to a certain extent accomplished incidentally wherever human dwelling are removed beyond the fly-range and wherever places of human concourse or traffic therein are cleared of undergrowth and the opportunities of the fly for feeding on human being are curtailed. I have mentioned that it has been observed that such places as native markets on or very near to the lake-shore are infested by swarms of flies, and that similar swarms are found at the habitual shore-resorts of such animals as hippopotami and crocodiles, probably as a result of a plentiful food-supply. Such haunts of these animals, therefore, as exist anywhere near human settlements or traffic-routes should be cleared and the animals either killed off or driven away and, since *Glossina palpalis* seems to be omnivorous as far as vertebrate blood is concerned, any vertebrate which may be found to offer it special opportunities for feeding should be got rid of, as far as possible, in like manner.

One of the first measures which occurs to one for the prevention of the spread of epidemics is the closure, complete or partial, of traffic-routes, but this is impossible in the present instance for special reasons. In the first place it could not be satisfactorily carried out, or could not be prolonged over a sufficient period, for the same reason that quarantine is inapplicable, namely, the long and indefinite duration, amounting sometimes to years, of the infection in human beings. Another reason is that it appears, so far as one can tell at present, impossible to find alternative main traffic-routes* which would have any prospect of being safer than those now in use, and that to open up new routes which are equally infested by fly would but widen the spread of infection in the long run. Then, again, practically all the more important traffic of the country is unavoidably connected somewhere or other with infected districts, and practically all the internal transport is done by porters who either are, or have been at some time, living in contact with epidemic areas. I may explain that, in speaking of traffic, the intercommunication between the natives themselves, whether for trade or other purposes, is included and forms, probably, a far larger proportion of the whole than that pertaining to non-native traders and travellers, and that of the Government combined. This would never be stopped nor to any great extent controlled by

* I allude to the internal traffic-routes of the Uganda Protectorate.

closing roads, but would filter through the country to the same extent as before and through more numerous and often more dangerous channels.

Probably the best that can be done in this direction is to establish some sort of control, by medical inspection and surveillance, of native travellers, traders and emigrants from epidemic areas, and especially such as wish to pass through or remain in districts in which the fly exists but has not yet been infected. In all such potential epidemic areas, if there remain any in the Uganda Protectorate, as is possible in the case of the northern part of the Nile Province and the region round Lake Albert Edward, it is very necessary that precautions should be taken; and emigrants, visitors and travellers should, wherever possible, be kept from contact with the fly-ranges in the same manner as is recommended for segregation of the sick, *e.g.*, by clearing ferries, fords, &c., on the main approaches; by fixing markets in the fly-free localities, as, for instance, the salt market in Toro. Like precautions should be taken in all places where efforts are being made by clearing and otherwise to stamp out the disease.

As regards the traffic-routes themselves, they have already been spoken of with reference to clearing. It must be borne in mind that roads do not pass through wide fly-belts, but they are infected, or liable to become so, in spots, strips and small patches, where they pass through or come in contact with fly-ranges on the borders of streams or lakes. The most practical plan seems to be to regulate and improve the present routes as far as possible and, in opening up new ones, to take every precaution in advance to make them as safe as circumstances will allow. In improving the present routes diversions may be feasible at some points, clearing will be necessary at others, especially at such fords, ferries, landings, camps and watering-places as the fly infests. In water-traffic the course should be, wherever possible, at least 50 yards from any shore or bank where the fly is known or believed to exist, and camping-places and fuel-stations should be carefully chosen and cleared, not only regular but also emergency camps being prepared, especially where sailing-vessels are in use. Another necessary precaution will be clearing of roads from camps to the villages where the porters' or sailors' food is obtained, if the way lies anywhere near the waterside, and it might be arranged that their food should be brought into camp wherever this is possible.

It is necessary, perhaps, to point out the fact that, in clearing a station or settlement or a ford or ferry on a traffic-route, the total abolition of every fly would, in many of the worst places, require more extensive clearing than has been recommended above, for stray flies may be brought in occasionally by native traffic through the bush, or, possibly, might wander, in some places, from neighbouring breeding-grounds. These last, however, we hope in the near future to be able to locate

and to deal with much more easily and radically than is the case at present. To banish the swarms of flies that at present infest such places in many instances is, however, comparatively simple, and we must remember that an occasional fly will neither cause nor serve to keep in progress a great epidemic, and that the risks of infection will be enormously diminished by such measures as have been recommended. The main difficulty will be the up-keep of the clearings which have once been undertaken, and this should be, with proper supervision, a constantly decreasing labour and expense as time goes on.

In conclusion, I may add that my personal opinion, which, though it may seem optimistic to many, is based on long and careful observation of the distribution and habits of the fly and of the distribution and extension of the epidemic, is that, in the Uganda Protectorate at all events, it is possible to control the spread of infection to a large extent and that, if it were not for the natural indolence, indifference and want of confidence in the natives themselves, the task would be far less onerous than it is likely to prove as things are. The natives, however, or at any rate the bulk of them, must eventually come to appreciate the wisdom of our advice and of our actions. When these begin to be attended by successful results they will cease to distrust our motives so that, if the present epidemic can once be checked, any future outbreak beyond those endemic centres which are unhappily almost certain to remain should be controllable with comparative ease.

I will now summarise the foregoing report very briefly as follows:—

- 1, The mapping of the distribution of *Glossina palpalis* in the Uganda Protectorate is practically complete, for, wherever it is not yet mapped, the physical conditions of its habitat are sufficiently well known to enable us to say with certainty whether or not the fly is likely to be found.
2. The distribution of sleeping sickness, which was pretty well known before, except in the case of the Nile Province and the small epidemic near Elgon, has been confirmed, and the observations appear to connect the disease more closely than ever with *Glossina palpalis*.
3. Broadly speaking the degree of infection and the distance of penetration (other things being equal) into the hinterland is everywhere proportionate to the intensity of the infection and the prevalence of fly at the corresponding lake-shore or river-side.
4. The enquiry has shown the limited extent of the "infective areas," in which alone sleeping sickness is communicable to man, and the wide extent of the fly-free interior, in which it is not communicable.

5. The "infective areas" form a very small proportion of the epidemic areas and the bulk of human infections is due to communication with these areas, while only a small minority is caused by actual residence within them.
6. Investigation shows also the efficacy of clearing when scientifically applied, the apparent feasibility of segregation, and the importance of obtaining native co-operation if possible.
7. By clearing or otherwise destroying the narrow "natural" range of *Glossina palpalis* the wider "following" range is abolished.
8. It is most important to consider, with regard to prevention, the width of the fly-ranges (infective areas) and the constant traffic with these from inland.
9. The most important and most practical preventive measures at the present time appear to be a combination of the clearing of and segregation from the infective areas, with or without deportation. Also the segregation in fly-free country will favour the administration of any special treatment.
10. Our action in the Nile Province, the Nile itself not being a true inter-tribal boundary and there being constant migration from bank to bank, must depend on the result of our enquiries into the capacity of *Glossina morsitans* and *pallidipes* of carrying the infection, and also on the action (if any) which may be taken by the Sudan and, especially, the Congo Free State Governments in the matter.
11. The natives of the Uganda Protectorate, by keeping their sick from the water-side, their dwellings outside the fly-range and their water supplies, fords, ferries, landing, markets, &c., cleared of undergrowth and placing them, wherever possible, in fly-free situations could, in all probability, themselves control the disease; and though it is not likely that the bulk of them will yet attempt it, it is possible that they may in the course of years gradually acquire a habit of using the defensive measures now proposed.
12. It is probable that sleeping sickness may remain endemic in certain parts of the Protectorate which will become localised as time goes on. Whether the lake-shore or Nile-bank regions will remain permanently dangerous to a population living in them will depend chiefly on the natives themselves.
13. It is most important that the duration of infection in the fly should be determined.
14. In the Uganda Protectorate, although it may be impossible to eradicate sleeping sickness in a few

endemic centres. I believe there is good ground for hope that the present epidemic may be so far controlled, over the greater part of its extent, that the disease, even though we fail to find an effectual and practicable cure, may cease to be a menace to the population and a serious obstacle to the development of the country, and, further, that fresh outbreaks of anything like the dimensions of the present one should become almost impossible of recurrence in the future.

APPENDIX.

I. ABSTRACTS FROM DR. BAGSHAWE'S AUGUST REPORT.

Experiments on Flight of Glossina Palpalis.

I was led to think that flies might be present in abundance at a spot far from their breeding-place if a constant supply of animal food were there obtainable, and to devise an experiment which would show how far flies may wander in the course of a river.

Trial experiment.—On August 7th 46 flies were caught at Harubale Ford and brought to the camp. I snipped from each with scissors a portion of the right fore-leg and put them into another cage.

Afterwards the 46 flies so treated were released at the ford. On the 8th 108 flies (47 males, 61 females) were taken at the ford, two of which had a portion of the right fore-leg missing, and were evidently two of those marked the day before.

Clearly here I had a ready means of identifying a retaken fly.

Experiment No. I.—On the 9th I sat at the ford while the boys caught flies. Each as it was caught was brought to me, held while I snipped off a part of the *left fore-leg* as nearly as possible through the tibio-femoral joint, its sex noted, and the fly put into a fly-box. Seventy-nine were so treated (21 males, 58 females). Three others were caught already maimed (on the 7th); these were killed.

In the afternoon I took the 79 maimed flies to hippo. landing-place 500 yards further up the river, at a spot where fly abounded, and released them.

On the 10th I similarly treated 113 flies (49 males and 64 females).

On this occasion I kept a special record of the flies which had followed the fly-boys (my station being 50 yards from the water) and which were caught on the spot: of these 12 were males and 19 females. It is interesting to note that one of these was a fly I had marked on the 9th, and that it was caught

by imprisoning the proboscis in a porter's skin with a scissor blade. Three others were flies marked on the 9th; they were discarded.

The 113 flies were released on the same spot as the 79, making a total of 192 flies marked in the same way (*left fore-leg*).

On the 11th 211 flies (92 males and 119 females) were caught at the ford; of these 10 males and 8 females were identified as flies released on the 9th and 10th, *i.e.*, of the 211 flies caught 18 had come from the spot 500 yards higher up, and of the 192 mutilated flies 22 had been recaptured, or more than 11 per cent. This result was decidedly encouraging: I resolved to vary the experiment.

Experiment No. II.—On the 12th I operated on the flies at the hippo. landing-place mentioned (to be referred to as "H."), snipping the left mid-leg through the tibio-femoral joint. 104 flies (43 and 61) were so treated: they were then liberated at the same spot. The 13th was dull: no flies were caught.

On the 14th there were caught at a fishing-hut (A) 400 yards below the ford (900 yards from H.) 101 flies, of which 1 male had the left mid-leg deficient.

At the ford were taken 113 flies (48 males and 65 females): of these 2 males and 2 females had the left mid-leg deficient, *i.e.*, 1 fly had wandered 900 yards from its original place of capture, and 4 flies had wandered 300 yards from their original place of capture.

The flies identified as marked on other days were noted and killed.

Experiment No. III.—On the 16th I marked at the ford, by dividing the right of the mid pair of legs through the tibio-femoral joint, 65 flies (22 males and 43 females).

On the 17th, at H., 109 flies (43 males and 66 females) were similarly treated. In the afternoon I took these and the flies marked on the 16th to a spot above the Mpanga waterfall, estimated by Mr. Haldane and myself as certainly a mile from the ford. Here were released nominally 65 males and 199 females, but several had died. The 18th was rainy and sunless.

On the 19th there were caught at the ford 429 flies (191 males and 238 females). Of these 2 males and 6 females wanted the right mid-leg, *i.e.*, on the 3rd day 5 per cent. of the flies liberated a mile away had been recaptured.

Experiment No. IV.—A repetition of No. III.

On the 22nd 89 flies (37 males and 52 females) were marked by the removal of the right hind-leg, taken to a spot above the fall and there released. A fly (female) caught during the operation had the right mid-leg wanting. On the way back to camp I visited the river about half a mile lower down in the gorge where it is difficult of access. Here 7 flies were caught, one of which was a female I had released half an hour before.

August 24th. Of 135 flies caught at the ford 1 male had the right mid-leg deficient.

August 26th. Of 199 flies caught 1 male and 1 female had the right mid-leg deficient, and 1 female had the right hind-leg deficient.

On September 2nd I visited Harubale from Kasunga. 163 flies were caught at the ford.

Two females had the right mid-leg missing, 1 had the right hind-leg missing.

Thus, of the 174 flies released above the fall on August 17th, 14 (4 males and 10 females) had been retaken a mile below, and of the 89 released on the 23rd 2 females had been retaken a mile below (time had not been sufficient for the last experiment).

These figures, as far as they go, tend to show that females fly further than males, but they are, of course, too small for definite conclusion. They show at any rate that flies will wander along a river such as the Mpanga a mile.

The natives nearest the Mpanga fall are those of Harubale. There was no question of flies following human beings, for to reach the village from the fall one is compelled to make a wide détour.

In the large number of flies I examined I noticed that a few had limbs missing, but in such a way that it was evident they were not flies marked by me. I was careful not to count these. In a few doubtful cases where I was inclined to discuss the matter with my "dresser," who always helped me, he would not admit of any doubt, and all such flies were rejected.

When I reached Bukarungu I carefully examined a series of 1,088 flies to determine what proportion had lost limbs from casualty or disease. I found that in one a fore-leg was gone; in six a mid-leg; in four a hind-leg.

In every case but one the whole limb was absent, so that one required a lens to clearly make out the stump (in the remaining case the limb had been divided through the tibia). One or more tarsi are of course often pulled off in manipulation.

In my experiments the whole of the femur was left, so that the correction for flies maimed by other agency than mine is so small as to be negligible.

It is evident that the finding of flies at any spot need not signify that their breeding-places are near: they might well be some hundred yards away.

With the approval of the Medical Officer-in-Charge I propose to repeat these experiments on a larger scale on the Semliki River.

Above the Mpanga Falls I found no fly, so that it may be argued that the 15 retaken flies had merely returned to their breeding-places.

It is noteworthy that of the 192 flies marked on the 9th and 10th 53, or 27.6 per cent., were retaken, and of the 104 flies marked on the 12th 28, or 26.9 per cent., were retaken.

*Discovery of Pupæ of Glossina palpalis in Natural
Breeding-Grounds.*

Pupæ, 51 in number, were found on August 29th and 30th at the camp half-way between Harubale and Bukarungu. They were lying in loose, dry, friable humus round and beyond the roots of cultivated bananas on a bank sloping to the lake at distance from the water varying from 4 to 20 yards. They were not numerous in any one spot, but required prolonged and careful search. The 51 represent the labour of 15 men for 3-4 hours on the 30th (one only was found on the 29th). One porter found 14 pupæ. Empty pupal cases were found in the proportion of 4-1 of occupied ones, and were nearer to, in some cases perhaps on, the surface. One pupa "hatched out" in a porter's hand as he carried it to my camp.

These bananas constitute a belt varying in width from 6-18 yards and about 100 in length. They are backed by dense, woody undergrowth, which extends 100-200 yards back from the lake. I have searched for pupæ in this undergrowth, but up to the present without success. I am engaged in further investigations. Amongst the bananas all that is necessary is to gently turn over or rake the humus with the fingers.

I have since found pupæ at Harubale amongst bananas close to the river 250 yards above the ford, and again at Bukarungu in bananas from 5-40 yards from the Nyamakoiyo, which here runs at the edge of swampy forest.

Under a shrub (*Allophyllus*) were found 39 occupied and 106 empty pupæ cases, and there were probably many more as the search was not exhaustive. A dry bank shaded by the *Allophyllus* and creepers which had spread over it, covered with vegetable débris and permeated near the surface by a network of rootlets, formed the nursery for these pupæ. The majority of the living ones were found at a deeper level than that at which I had sought them before. If one found empty cases near the surface and prised up pieces of earth with a finger, one came sometimes on a nest of three or four living ones close together. On the 10th, after a search in many parts of the woody undergrowth at the river bank, I found pupæ on a steepish slope above the hippo-path, and seven empty cases. One may for the present say that the larvæ are dropped in shade, it may be of shrubs, it may be of bananas, within 45 yards of water, on banks with a decided slope where the surface-soil is loose and friable and partly composed of vegetable débris. The slope seems essential. The natives who helped me in the search always looked for a bank.

*Breeding Grounds and Pupæ of Glossina Palpalis.**

The discovery of the breeding grounds by Dr. Bagshawe is most interesting, and may prove to be very important indeed in dealing with the fly and its haunts. If, for instance, the breeding grounds should prove to be confined to definitely circumscribed areas in which the pupæ can be discovered without very great difficulty, or if these localities can be fairly readily recognised by their characteristic physical features or by any other means, this fact would be likely to limit to a considerable extent the areas necessary to be dealt with by clearing and planting, and would thus reduce the expense of dealing with such areas. If, in short, we could attack the breeding places in the same way as we do those of the mosquito, our task would be much lightened and simplified. If, on the other hand, the pupæ are found to be deposited in a more or less haphazard way along suitable foreshores, we shall remain in much the same position as we were before, and must hope, in clearing the natural range of the fly, to destroy the breeding places at the same time.

The fact of the pupæ having been first discovered in a banana plantation should not be allowed to associate these plants unduly with breeding places in the minds of investigators. More or less of a bank, loose earth with vegetable debris, and shade, are evidently the chief requirements, and the fact of the banana plants affording the last will probably prove to be exceptional in most localities.

The experiments on the longshore flight of *Glossina palpalis* are most interesting and ingenious, and give valuable information. The limits of flight along shore or bank, however, must be carefully distinguished from the flight inland or across water,† which is much more circumscribed. It must be taken that the distances of flight recorded in the experiments refer to a river bank along which there was practically continuous shade. Cleared spaces have been found to form breaks in the fly distribution, and further experiments are needed in order to show what extent of shadeless or cleared bank is necessary to form an efficient barrier to longshore flight.

The experiments show how important it will be, in clearing banks and foreshores, to destroy the breeding places, since a cleared foreshore, if flanked on either side by long stretches of shaded foreshore, will probably be continually invaded by fresh flies as often as ever the undergrowth in such a clearing is allowed to make any headway. They also point to the manner in which seasonal variations in the number of flies can occur on rivers or lake shores in accordance with the varying physical conditions of shade, water level, &c., which from time to time prevail.

* Note by Dr. Hodges.

† That is, the "fly-range," as understood in this report.

Apart from the ordinary physical conditions necessary to a fly area, the number of flies infesting any given spot must depend chiefly on food supply (*e.g.*, native markets and traffic, crocodile or hippopotamus banks, &c.), and when such places are cleared we diminish food supply, and must eventually decrease the actual number of flies. Any point on a bank or foreshore at which human or vertebrate blood is available as a food supply will be infested, until it is cleared, by flies from any or every breeding place within the limits of longshore flight, and not separated from it by a cleared or fly-free interval of sufficient extent to form a barrier.

II. SEGREGATION AND TREATMENT BY MEANS OF ATOXYL.

In this appendix I include copies of my letter, No 78/S.E.E., to His Excellency the Commissioner, and No. 81/S.S.E. to yourself, dated October 20th and October 25th, 1906, respectively, which allude to His Excellency the Commissioner's scheme for segregation and to my proposal to combine with it treatment by means of atoxyl.

His Excellency's scheme of segregation includes, in brief, besides segregation of the sick, deportation of reputed sound persons from a zone of two miles from the lake shore from all such places as are dangerous or such as it is impossible or unnecessary to deal with by clearing. These people will not be compelled to live at any particular place or places, but must be removed to fly-free country, and, as far as possible, will go to the inland estates of those chiefs on whose lands they have previously lived, where they will form, it is hoped, new and healthy settlements.

Such a procedure as this, it seems to me, is the only one approaching to thoroughness by which we can hope to check for the time the extensive and omnipresent traffic which radiates from the lake shore, and which is shown in the above report to be responsible for the great bulk of the infection in this epidemic. This traffic, which shows an enterprise most creditable to the natives concerned, and which, apart from sleeping sickness, would be of the greatest use in developing the country, need not, it is hoped, be indefinitely stopped or even greatly curtailed, but, for the present, it is imperatively necessary to check it as far as possible, especially since, so far as it affects the food supply and the necessities of existence, it is nowhere and by no means indispensable, unless it may be to some of the islands, for which special arrangements can be made if it be found necessary.

(Enclosure 1.)

(No. 78/S.S.E.)

SIR,

Entebbe, October 20, 1906.

I HAVE the honour to inform you that, in view of the success recently reported from Europe in the use of atoxyl as a cure for sleeping sickness, and of the hopeful opinion as

regards its curative properties, expressed personally by Professor Koch, the distinguished head of the German Sleeping Sickness Commission, I consider it advisable, although no certain cures can be scientifically demonstrated for some considerable time, and possibly for some years yet, that measures should be taken as soon as possible to test this drug on a large scale among the natives of the Uganda Protectorate.

For, whatever may be the ultimate result as regards cure, it is certain that preparations of arsenic are beneficial and often lengthen life in human trypanosomiasis, besides lessening the risk of infection by banishing the trypanosome from the glands and peripheral circulation, so that such cases for the time being cannot infect the fly and cease to be a danger to the community. It is a fact also that atoxyl is a less poisonous preparation of arsenic than any hitherto known, and can, for this reason, be given in larger quantities, is safe and suitable for hypodermic administration, and is far more applicable for general distribution among the thousands of sick natives with whom we have to deal than any drug which has previously been proposed as a cure.

I consider, therefore, that not only is it justifiable to incur very considerable expenditure in giving it an extensive trial as a curative agent, but that the measures undertaken for this end may be so ordered as to assist materially in carrying out the most important general measure which is at present open to us, namely, segregation of the sick, which His Excellency has now in contemplation.

I would suggest, then, that a central camp be chosen and prepared in advance in each important county or district affected by sleeping sickness; that such camps be situated in fly-free country, of which the Sleeping Sickness Extended Investigations have shown that there is plenty to choose from in the interior, and that they should be at a sufficient distance outside the nearest fly-range to minimise both the expense of strict policing and also the appearance of constraint, by making it difficult for irresponsible and demented patients and others to wander back into the infected zone.

I would also suggest that all buildings and shelters at these camps be of a temporary nature, so that a camp could be shifted easily and without much expense if necessity arose, as, for instance, the outbreak of some other epidemic such as small-pox, the occurrence of insanitary conditions or the insufficiency of food or water.

Since there is plenty of safe country from which to choose, the selection of sites need only primarily depend on medical and hygienic conditions and their exact location would be determined by administrative reasons and native interests. As regards sleeping sickness the following centres would be advantageous:—Northern Busiro, Northern Kiadondo, Northern Chagwe, Northern Mawakota or Western Buddu, West-Central

Busoga, the neighbourhood of Masindi (for Unyoro), the neighbourhood of Fatiko (for Nile Province), and the centre of Buvuma for the Northern Group of Islands, this last being necessary if we are to avoid an inrush of islanders, of whom a very large number (perhaps 80 per cent.) are already infected, into the less highly infected mainland.

The German Sleeping Sickness Commission has already its camp established in the Sese Group, and will probably be able to serve that district for the present as regards treatment. The duration of its stay is, however, unknown, and in any case its camp cannot serve the purpose of segregation, so that later on an additional camp will be needed for the Sese Islands.

The construction and management of these camps would be adapted to segregation, and they could ultimately become villages or settlements rather than camps. The question of food will be an important one to be considered, especially in fixing sites, but as a general rule Government could only supply free food to such patients as are helpless and without friends.

I feel sure that if their proposed use for atoxyl treatment were published among the natives, such camps would have great attractions for all those sick people along the fly-infested lake shores and river banks whom we wish to segregate and would form the safest means of segregation at our disposal, since all will probably be anxious to avail themselves of the new medicine, of the comparative success of which many of them have already heard rumours.

I do not propose that the atoxyl treatment be carried out on the lines of strict scientific experiment and investigation at more than one of these camps, since for this a much larger increase of staff would be required than is here contemplated, but it would be necessary to have one experimental camp, which would probably be the one in North Busiro. This would be started first, and, as soon afterwards as the necessary staff becomes available, camps for atoxyl treatment and segregation might be opened in the following order:—Unyoro, Usoga, Buvuma, Chagwe, Kiadonda, Buddu or Mawakota, and the Nile Province. This last would probably be for treatment only, since it is doubtful if segregation would be possible there.

In all I have recommended nine camps or centres, including that which will eventually be required for Sese. In order to place all these in working condition I estimate that an increase of at least five temporary Medical Officers will be required, and, in view of the fact that this work, if undertaken, should be commenced as soon as possible, and carried on without break or hindrance, and that three of the Medical Officers at present engaged in the Sleeping Sickness Extended Investigations will be due for six months' leave in April and May next, I consider it necessary that the services of these extra Medical Officers should be available in Uganda by April, 1907, at the

latest. In making this estimate I allow two Medical Officers for the Investigation Camp and one each for the eight Treatment Camps, as I consider that, for treatment only, not more than one European will be required to take charge of a camp. This staff of Europeans, if kept at constant strength, constitutes the minimum which will be needed for the efficient carrying out of the medical work proposed. It is impossible to say, until the details of the administration of these camps can be worked out, whether the Medical Officers in charge will be able unaided to undertake it in addition to their other duties.

A subordinate staff, consisting of one hospital assistant and eight compounders (Indians) (see Note 3), will be needed, the first for the Investigation Camp and the others for the Treatment Camps, at each of which the Medical Officer will require an assistant who can read and write and help both in the care of cases and in the keeping of records. Whatever treatment might be adopted and whenever its use may be undertaken, arrangements very similar to the above would, in my opinion, be inevitable. The scheme of segregation now in contemplation by His Excellency needs such arrangements and appears to me altogether advantageous for the purpose of treatment on an extensive scale.

On account of the many thousands of the sick and of the vast area over which the disease is spread it would be essential, under any circumstances, to have at least as many centres of operation as I now propose, while it would be equally necessary to fix them outside the fly-range, since any concentration of persons for whatever purpose within the infected area would lead to disastrous results in the further spread of the disease.

In such camps as I have named there would be no danger whatever of infection to the Medical Officers and attendant staff, nor, indeed, to any non-infected person; and for this reason there is no need to choose sites far removed from centres of population and cultivation, so long as these are free from *Glossina palpalis*. It will, on the contrary, generally be advantageous to be near such centres, on account of the facilities they offer for obtaining a plentiful supply of food and other necessaries for the sick people.

I have, &c.,

AUBREY D. P. HODGES,

Medical Officer in Charge.

Sleeping Sickness Extended Investigations.

NOTE.—November 18, 1906. Nine hospital assistants would be much better and more useful if they can be obtained. I calculate, with reference to European staff, that two European Medical Officers should, if possible, be retained for the present on travelling investigation to complete the enquiries which are being made, or until this class of enquiry is completed.

(Enclosure 2.)

(No. 81/S.S.E.)

SIR,

Entebbe, October 25, 1906.

I HAVE the honour to inform you that, His Excellency the Commissioner of the Uganda Protectorate having taken up the scheme of segregation of the sick for the prevention of the spread of sleeping sickness, it seems to me that the same arrangements which will be required for applying this may be most advantageously used for an extensive trial of the atoxyl treatment, of the success of which there have been reports both from Europe and from the German Sleeping Sickness Commission.

I have therefore sent to His Excellency a proposal, a copy of which is enclosed (No. 78/S.S.E. of October 20th/06), for these two measures to be carried out conjointly.

You will see that a considerable increase of the staff of the Sleeping Sickness Extended Investigation will be needed for the segregation camps, but I do not think that the use of the atoxyl treatment will, apart from the segregation scheme, lead to any serious expense beyond that for the purchase of the drug and a few necessary appliances.

You will see also that a large quantity of atoxyl will be required, since the patients at each camp will probably number thousands, and I consider it most important to obtain a good supply immediately, so that the two measures can be combined as nearly as possible from the start, and that they may be begun while the natives are still in the enthusiastic humour in which they appear to be now of presenting themselves eagerly for this treatment.

* * * * *

I have, &c.,

AUBREY D. P. HODGES,

Medical Officer in Charge,

Sleeping Sickness Extended Investigations.

To the Principal Medical Officer.

III. INSTRUCTIONS TO MEDICAL OFFICERS ENGAGED IN THE EXTENDED SLEEPING SICKNESS INVESTIGATIONS.

February 20, 1906.

The initial steps to be taken in this investigation will be the minute study of the distribution and habits of *Glossina palpalis* and of the areas which have become, or are likely to become, infected with sleeping sickness.

By these studies, carefully carried out, an exact knowledge should be gained as to the co-existence or otherwise of the disease with this particular fly and, therewith, sufficient data to determine the possibility of the existence of other means of

dissemination. Valuable information should also be acquired as to the probable directions in which the epidemic may in future spread, as to the likelihood of small or large outbreaks occurring in different localities and as to what, if any, general hygienic or administrative measures would be likely to be successful in preventing its extension.

Special attention should be given to the feasibility of local segregation of the sick from fly-infested villages or circumscribed fly-areas by the natives themselves, since there is reason to hope that in many cases this could be done through the local chiefs with little trouble or expense and without incurring the opposition, sentimental or otherwise, of the natives.

By the use of tact in the inspection and examination of natives and by giving them medical treatment for their ordinary ailments, their confidence should be so far gained that later on systematic blood and gland examinations and special systems of treatment for sleeping sickness may be carried out among them with much greater chance of completeness and experimental success than could be hoped for at present.

The following paragraphs explain in detail what is included in the measures indicated above, and contain information relating to methods of investigation, &c.

1. The term fly-belt has as yet no exact meaning, and should not therefore be used in descriptions or on maps. *Glossina palpalis* is known to frequent localities near the water where there is shade. It is probable that there must be some, however little, *open* water in these localities and some conformation, such as rocks, shelving beach, cliffs or high banks, which ensures a moderate dryness for a great part of the year, and it would seem that wide belts of swamp-vegetation, such as papyrus, behind which is no open water, though often plenty of shade, are inimical to its presence. All these last points require confirmation. The localities infested by the fly, called herein fly-areas, vary much in extent. They may be quite small, circumscribed and isolated, or many such areas may form more or less continuous chains for considerable distances along the borders of lakes or rivers. It is important that the limits of these areas or groups of areas should be accurately ascertained before any general measures such as local segregation can be carried out. Also, the fly is known to follow water-carriers and others for some hundreds of yards. It is necessary to determine how far from their usual haunts flies will travel in this way, how far they may wander under other circumstances, and, especially, how far from water their haunts or areas may be situated. Thus specimens for identification should always be obtained and sent in in case tsetse are met with at any considerable distance from water, since some species, notably *Glossina morsitans*, are frequently so found, and it is probable that in many instances in which the presence

of tsetse has been reported at a distance from water the species was some other than *palpalis*. During recent investigations in Unyoro and the Nile Province the fly-areas were always found to be close to water and circumscribed. On approaching such an area a fly was seldom seen much more than 50 yards from the water, though on leaving it they were sometimes observed to follow for a distance which never exceeded 200 yards. Tsetses which were caught at a greater distance from water than this were invariably *G. morsitans*.

2. The fly-areas, then, should be carefully mapped out and the physical conditions prevailing in each as regards shade, rocks, cliffs, distance from open water, stream, swamp, &c., should be noted, compared and tabulated for report; and the fly-range, or distance which it may wander from its actual haunts, should be determined.

3. With the appearance of *G. palpalis* medical officers are familiar. In its flight and manner of settling it resembles other tsetse flies. The former is rapid and direct and it settles abruptly, as a pellet of mud sticks when thrown against a wall, yet so gently that it is scarcely felt. There is no hovering and little or no movement from the point of settling before it bites or is driven off. Its buzz is a continuous note broken only when it alights.

4. All the habits of the fly should be carefully observed, its numbers in the various fly-areas and its local distribution, especially as regards the proportion of males to females. In localities in which this proportion has been studied the males have been found to preponderate largely, and this fact may be connected with its breeding-habits. Whenever wandering or following flies such as have been alluded to above are taken, the sex should always be determined.

5. The hours of the day during which *G. palpalis* is active are not yet accurately known. In some places and at some seasons, at any rate, it does not begin to attack till the sun is well up, it is rarely seen after 5 p.m., and it is met with in greater numbers on bright sunny days, whereas *G. morsitans* may attack fiercely before daybreak, is often most voracious about sundown, and has been said to prefer dull weather.

6. Investigations should be made as to the natural food of *G. palpalis*—whether vegetable juices form a part of it and what animals besides man it habitually attacks, especially water or water-side mammals, birds and reptiles, of which blood-smears should be obtained whenever possible. Some of these should be examined fresh, and others dried and sent in for examination. Observations as to feeding (*e.g.*, on crocodiles or hippopotami) could sometimes be made with the aid of binoculars.

7. Special efforts should be made to discover breeding-places and where larvæ and pupæ are deposited and concealed.

Medical Officers are recommended to search cracks and crevices in rocks, dry earth, dead wood and the bark of trees. Sand and loose earth and grass or other vegetation should also be examined. Pupæ are perhaps more likely to be found somewhere above the high-water mark of rivers, &c.

8. Little is known as to the seasonal absence or variations in numbers of the fly in a given locality. This should be studied. In some cases information on this head may possibly be gained from natives, but very often the fly is barely known to them. Where there is a local name for it, this should be recorded. Among the Baganda it is called *ki'vu* (plural *bi'vu*) and among the Bachopi in N. Unyoro it is known as *malingwa*, these names probably including all tsetse flies. Others, such as the Banyoro and the Nile tribes, have names which include all biting flies, varying only with the size of the insect.

9. Specimens from each fly-area, male and female, should be collected and sent in as soon as possible after capture for identification. Males may be distinguished by the oval protuberance on the ventral aspect of the hinder end of the abdomen, which is placed longitudinally. Each fly or set of flies must be clearly labelled with the date and locality of capture and the approximate distance from water (*e.g.*, close, 50 yards, 200 yards, &c.). In the case of flies caught in the early morning or late evening, the hour of capture should be added.

10. The surest method of capture is to wait quietly near the water's edge (or wherever the fly has been seen or heard) either in the shade or in a small open space. It is well to have one or more natives waiting in front of the observer. It may be necessary to wait for half an hour to an hour or even a little longer before one is caught, though with a little practice its presence may be detected long before this by its buzz or its peculiar manner of settling. It will more readily settle on the lee side of its victim and on the shaded parts, such as under the chin in man or behind the knee in the sitting posture, and on the under parts of animals. It would be well to determine whether it can bite through clothes, for it certainly attempts it.

11. The greatest care should be taken in drying and packing flies, as, if they cannot be identified, this may entail in some cases serious waste of time and labour in going over the same ground a second time.

Specimens should be packed in glass tubes, but, if the supply of these should fail, pill boxes may be used. In either case sufficient tissue paper should be inserted to prevent damage to the flies by shaking. To prevent mould it is a good plan before packing to dip them in 1 in 40 carbolic and then to dry them quickly in the sun on blotting-paper, taking care that they are not carried off meanwhile by ants, &c. The tube,

also, should be sterile and thoroughly dry, and gorged flies should not be packed with others, as they would probably putrify and spoil the whole consignment.

12. Other biting insects should also be collected. Flies may be packed as above, but not in the same tubes or boxes with tsetse Ticks, &c., should be placed in $2\frac{1}{2}$ per cent. formalin or weak spirit. Any observations on biting insects which may bear on the present investigations should be embodied in the reports.

13. Fresh ungorged flies should be examined microscopically to determine whether they carry trypanosomes and, if so, in what percentage of captures. This should be done both in infected and in apparently non-infected fly-areas, and the method recently employed by Dr. Koch of squeezing out the contents of the proboscis on to a slide should be adopted, as well as examination of the abdominal contents.

Should trypanosomes be found in this way dry preparations should be made, not only from the proboscis but also from the alimentary tract, and sent in for examination, to determine if possible the nature of the trypanosomes present.

14. Freshly gorged flies should be captured and examined to determine the kind of blood (mammal, bird or reptile) on which they have fed, and from these also dried films should be sent in.

15. Two of the most important questions at the present stage of the investigation of sleeping sickness are, that of the occurrence of a cycle of development of the trypanosome in *G. palpalis* and that relating to whether the trypanosome of sleeping sickness can be carried by other species of tsetse flies. Any observations or experiments which medical officers may be able to make, or any material they may be able to send in which might assist enquiry on these heads may prove to be of the greatest value.

Another question which may prove to be of importance is that of the relative infectivity of male and female flies. On this point it will be more difficult to carry out any research, but any information bearing on it will be of great interest.

16. Maps will be supplied, which should be amplified and and corrected where necessary, with the aid of local officials of the administration, who will be able to assist in fixing the location and in the naming of villages, streams, &c. On these maps the extent and position of the various fly-areas and of sleeping sickness epidemics will be indicated as exactly as possible, the former by red and the latter by black dots.

17. Local epidemics of sleeping sickness are to be enquired into, mapped and reported on with respect to origin, imported and local infection, number and proportion of persons attacked, the relation to fly-areas, the nature and frequency of communication with neighbouring fly-areas, the occupations of the natives, the probabilities of the spread of infection as regards

direction and the possibilities of large or small outbreaks resulting in various districts.

Recent epidemics or recently infected villages will demand most careful study, especially as regards origin and the transmission of infection to or from surrounding fly-areas.

A numerical record should be kept of the sick in epidemic areas, distinction being made between imported and locally infected cases and between the stages of the disease in which cases are found at the time of investigation.

18. Cases of sleeping sickness occurring in persons (especially children) alleged or supposed never to have visited an epidemic or infected fly-area should be examined and enquired into with the utmost care and reported fully by name.

19. Special investigations should be made as to how far it might be practicable, in each epidemic area, by removing huts or villages for a short distance (*e.g.*, from a river-bank to the next hill-side) to place them outside the fly-area, and also, by supplying the sick with water and perhaps other necessities obtained within the fly-area, to keep them from contact with the fly.

Such measures would greatly reduce the risk of infection wherever they could be carried out, for, although the apparently sick form only a proportion of those actually infected, they afford immensely greater opportunities to the fly, and, further, it has been suggested recently by Koch that probably only advanced cases are able to infect the fly.

20. Examination of the lymphatic glands should be systematically carried out both in populations living in connection with infected fly-areas and in those living entirely outside such areas. It should be remembered that in sleeping sickness the enlarged glands are soft to the feel, somewhat like a ripe damson, and are not hard and shotty.

21. Examination for trypanosomes by gland puncture should be made where feasible, but medical officers should proceed with caution in this matter till they have gained the confidence of the natives (see paragraph 23). One dozen spare needles will be supplied with each hypodermic syringe, so that a separate one can be used for each puncture, the needles used being afterwards sterilized by boiling.

A good method of procedure for the operation is as follows:— Draw into the syringe a little 1 per cent. citrate of potash solution and eject it again, leaving the inside of the syringe and needle moist; then puncture the gland, move the needle about slightly in the gland, draw out the piston, disconnect the syringe from the needle, withdraw the needle, attach the syringe again and blow out the contents of the needle on to a slide. A thoroughly clean slide and coverslip are essential.

22. It is most important to enlist the sympathy and interest of chiefs and other natives of influence. Opportunity should

be taken to acquaint them with the appearance and habits of *G. palpalis*, and specimens should be shown in order to test or aid their knowledge of them. The connection between the fly and sleeping sickness should be explained,—how the one is probably powerless to spread the disease without the other, and how important it is to remove huts and villages from within the actual fly-areas and to prevent the sick from remaining in or even visiting such areas, wherever such measures appear possible. Special stress should be laid on the fact that the fly is harmless unless it can bite the sick. It is important also to explain to them the intentions of the Government, which wishes to prevent disease and to see the natives numerous and well-off, and a point might be made of the large sums of money being spent for these objects. As the native immediately seeks a motive to explain any action which he cannot understand, and as he has great difficulty in understanding that Europeans (or others) would do him a good turn for nothing, that is, without some immediate selfish end in view, investigators may, unless care be taken to explain, just as likely be credited with the intention to spread, as with the desire to prevent, sleeping sickness. Any misunderstanding of this nature even in one district would be likely seriously to affect the whole field of enquiry, and cannot be too carefully guarded against.

23. Every effort should be made from the outset to conciliate and gain the confidence of the natives, who should be dealt with as far as possible through their local chiefs. Methods of observation such as gland-puncture should be used at first with caution and discretion, and in no case arbitrarily or without permission. But an attempt should be made to accustom the people gradually to such proceedings, so that later on their use may become more generally applicable and so of greater scientific value.

A patient attending for treatment of an ordinary ailment, for example, might readily submit to gland-puncture, whereas a person casually encountered in a village might strongly object. Again, though the glands in the neck are the most generally adapted for puncture, yet sometimes a patient who objects to puncture in the neck, an operation which he cannot see, will offer no objection to puncture of his supracondyloid glands, a process he can watch, and, since these glands are quite frequently enlarged in sleeping sickness, and yield trypanosomes when punctured, advantage might be taken of this fact.

24. The use of rewards or gratuities should be avoided as a rule, and it will be found less expensive in the long run, as well as more advantageous, to use them in the case of voluntary interpreters or guides who may have gone out of their way to give information and assistance rather than to actual patients. It may, however, sometimes be required to reward patients as being the first to come in or to submit to operation or examination, or the price of food may have to be supplied

to such as come from a distance and are kept for a short time under observation. A supply of pice should be carried for these purposes.

25. All provisions and commodities obtained locally from natives should be paid for at the local rates.

26. All expenses, including transport, are chargeable to a special fund under the head "Special Expenditure, Sleeping Sickness," and money can be drawn from Collectors locally by vouchers under this head. Exact accounts of all items are to be kept, and cash-books will be provided. It will be understood that strict economy is to be used.

27. Medical officers should seek the co-operation of officials of the administration and avail themselves to the utmost of their local knowledge and experience of the natives. Their advice or assistance with reference to such matters as roads, maps, guides, interpreters, local prices of native food, local native prejudices, occupations and methods of communication should be of great help in conducting the investigations.

28. It has been arranged that interpreters for the local dialects or languages will be supplied wherever possible by the local administrative officials. This is of the first importance both for facilitating the work and for gaining the confidence of the natives. Different interpreters may be required or be available for different parts of the same province.

29. Medical Officers should pitch their camps outside of actual fly-areas. In so doing they will find, as a rule, no difficulty in keeping in close touch with the investigation they have in hand.

30. Reports are to be forwarded, as soon as possible after the end of each month, to the Medical Officer-in-Charge of the Extended Sleeping Sickness Investigations, Entebbe.

These reports should describe the movements of the Medical Officer during the month and the observations and investigations made. They should also show the whereabouts of the Medical Officer at the time of writing and indicate the probable cause of his movements during the ensuing month, and they should include a statement of cash account.

In reporting their investigations, Medical Officers should follow in substance the exact order of the paragraphs in these instructions, using the corresponding numbers. But, although it is intended that the lines and methods of investigation indicated in them should be uniformly followed, there is no intention to limit in any way the field of research. It is hoped, on the other hand, that the accumulation of fresh facts and observations may serve to direct and guide the course of future enquiry and may lead to new and improved methods.

Any new fact or discovery bearing on the investigation of sleeping sickness should be reported immediately and separately.

31. Care will be taken that each medical officer shall receive the credit due for his own observations and discoveries, but the publication of any matter directly or indirectly connected with the investigations cannot be permitted without previous submission of it to the Medical Officer-in-Charge for his approval.

NOTE.—Further instructions with regard to paragraph 26 will be issued as soon as the details are arranged.

AUBREY D. P. HODGES,
Medical Officer in Charge,
Sleeping Sickness Extended Investigations.

24. REPORT ON THE SLEEPING SICKNESS CAMPS, UGANDA, from December, 1906, to November, 1907.

BY CAPTAIN A. C. H. GRAY, R.A.M.C., Medical Officer in Charge of the Sleeping Sickness Extended Investigations.

INTRODUCTION.—Despatch from HIS MAJESTY'S COMMISSIONER, H. HESKETH BELL, G.M.G., to the Secretary of State.

Government House, Uganda,
December 9, 1907.

MY LORD,

I HAVE the honour to submit a short report showing what progress has been made, so far, in carrying out the proposals, indicated in my despatch, No. 218, of 23rd November, 1906, for dealing with sleeping sickness in Uganda. For facility of reference, a copy of the despatch quoted is annexed.

2. It will be remembered that, with the concurrence of my medical advisers, I recommended that the whole population of the fly-infested shores of the Victoria Nyanza should be moved inland to fly-free areas, and that all persons found suffering from sleeping sickness should be interned in "segregation camps" where they would be medically treated. The use of atoxyl was to be given a special and exhaustive trial.

3. The whole project may, I think, be suitably divided into two heads:—

(1) Administrative measures, intended to prevent the spread of the disease;

(2) Medical measures to cure those already afflicted.

4. Relying on the opinions of the medical experts, to the effect that the disease cannot be spread by infected persons in localities where the tsetse fly (*Glossina palpalis*) is not to be

found, all natives, whether infected or not, have been cleared out of a two-mile belt all round the lake shore, and have been allowed to settle inland in fly-free districts.

5. I am happy to be able to report that this step, which might possibly have caused much trouble, has been carried into effect without the slightest difficulty. The chiefs, to whom the *raison d'être* of the whole scheme had been carefully explained, gave very loyal assistance, and on being assured that the tenants on their lake-shore estates would not be irretrievably dispersed, they put no obstacles whatever to the execution of the plan. All along the whole of the border of the lake—from Buddu to the Ripon Falls—the peasants have evacuated their holdings, and have been moved to suitable properties owned by the chiefs further in the interior of the territory. Their huts have been burnt, and their plantations of bananas have gone to waste. Only the seriousness of the whole situation could have warranted such drastic measures, and the docility with which our orders have been carried out speaks volumes for the respect in which the authority of the Government is held. A small amount of pecuniary compensation is being given in respect of each homestead destroyed, and I have reason to believe that no serious animosity has been aroused by our action in this connection. The lower classes in Uganda have always been so thoroughly under the control of their chiefs that the idea of resistance to the wishes of the Government in this matter doubtless never entered into their minds. The chiefs, whose opposition might perhaps have been almost insuperable, have, as I have already stated, loyally helped us even in cases where the necessary measures entailed on them some pecuniary loss.

6. If the experts on sleeping sickness be correct in their belief that a tsetse fly only retains the power of transmitting infection during a period of 48 hours, we may, therefore, now assume that every fly along the lake shore that has been unable to acquire fresh infection, is to-day as innocuous as it may have been before the introduction of sleeping sickness into Uganda. So long as infected persons can be kept away from fly-infested areas, the fly will presumably remain harmless, and it therefore now remains for us to take such measures as will ensure the continuance of their freedom from infection.

7. The situation in the Sese Islands and in Buvuma is far less satisfactory. The islands are small, their shores are densely wooded, and tsetse flies are terribly abundant. The people live largely on fish, and it will be almost impossible to keep them away from the water side. Dr. Van Someren estimates that, out of the six or seven thousand persons now remaining on Buvuma, 95 per cent. are infected with trypanosomiasis, and it is believed that the proportion in the Sese Islands is about the same.

8. The chief danger of finding nullified the measures which we have taken on the lake shore of the Kingdom of Uganda lies in the constant communication that exists between the islands and the mainland. The islanders have always been in the habit of bringing their fish, pottery, and other products to the mainland of Uganda and Usoga, and their canoes are constantly plying to and fro. Most of these canoe-men being infected, it would follow, in the absence of proper arrangements, that the flies on the shore of the mainland would be constantly able to find fresh sources of infection, and their newly-gained harmlessness would be open to much doubt.

9. I find it impracticable to order the rigid quarantine of the islands, and so as to minimise the risks referred to above, we have forbidden all traffic between the islands and the mainland, save at two or three properly defined places on the lake shore. These landing places are being thoroughly cleared of all trees and bush, and will thus be completely freed from tsetse fly. The clearings are of considerable width, and persons will be able to attend the markets held there without risk of being infected by the afflicted islanders.

10. The efficacy of these measures will depend very largely on their rigid and consistent observance, and I have detailed a special officer to see that they are thoroughly carried out. He will constantly travel through the belt which has been cleared of natives, and will assure himself that the old holdings and plantations are not reoccupied. He will also strictly supervise the traffic between the islands and the mainland, and will see that the authorised landing places and markets are kept perfectly free of fly. One of the Assistant Collectors, Mr. Haddon, has volunteered for this duty, and the necessity for taking proper precautions with regard to his own safety has been duly impressed upon him.

11. The collection of rubber in the two-mile belt has been prohibited, and it is possible that some small claims for compensation may be made by one or two persons who hold permits for this industry. The matter, however, is not of much importance.

12. The measures taken with regard to the fly-infested shores of Usoga are not so far advanced as they are in Uganda proper, but very satisfactory progress is being made there, and we hope that, in a few weeks, the border of the lake will be entirely free of people.

13. I am happy to be able to state that the measures adopted to drive the tsetse fly away from the townships of Entebbe and Jinja have proved entirely successful. The belts of citronella grass that have been planted along the shores of the lake at those places are evidently very distasteful to the *Glossina palpalis*, and a fly is hardly ever seen in their vicinity. I may add that these plantations of citronella show promise of giving

a remunerative yield of essential oil, and a distilling apparatus is now being procured.

14. It may, I think, be considered that, with the removal of the population from the lake shore, and with the maintenance of proper regulations for preventing the re-infection of the tsetse flies in the prohibited belt, the purely administration side of the problem has been, in some measure, satisfactorily dealt with. The medical side now remains for consideration.

15. The scheme for the suppression of sleeping sickness, which I ventured to propose in my despatch, No. 218, of 23rd November, 1906, was submitted to a committee of medical experts in London, and in July last it was decided that my recommendations should be adopted. On the 4th of July the Acting Commissioner was authorized to proceed with the projected camps in Chagwe and Usoga, and the final sanction for the whole scheme was telegraphed to him on the 15th August. I had, however, assumed the personal responsibility of commencing repressive measures as far back as November, 1906, and the Busiro Segregation Camp (since known as the "Buwanuka Camp") was opened in December on a tentative and experimental scale. The removal of the people from the lake shore was also commenced at about the same time.

16. Dr. Wiggins was placed in charge of the Buwanuka Camp, and by the end of April, over 300 souls were sent there for treatment. Dr. Wiggins went on leave and was replaced by Dr. Densham. On the 1st of June that officer was killed by a buffalo, and was replaced by Dr. Van Someren who, in August, was relieved by Dr. Collins. It is a matter for regret that such frequent changes in the medical staff should have been unavoidable, and I hope that, in future, it will be possible to leave the patients under the continued care of the same doctor.

17. At the end of July a segregation camp was established at Bussu, in Usoga, and Doctor Baker was placed in charge of it. In October he was joined by Lieutenant Archibald, R.A.M.C. This camp seems to be a popular one among the natives, and the admissions of sick people at the present date amount to 328. The death-roll up to the end of October showed 23 deaths.

18. Owing to the lack of Medical Officers the camp at Kyetume, in Chagwe, was not opened until August. This camp is under the charge of Doctors Van Someren and Bayon, and is also proving popular. The admissions during the last four months number 326, of whom only 18 have, so far, died.

19. A fortnight ago, a fourth camp was started on the largest island in the Sese group, and Dr. Goodliffe has been placed in charge of it. It is in the neighbourhood of the spot on which the German Commission under Professor Koch worked, and great numbers of the people there have already been under a variety of treatments.

20. I attach a copy of a report by Captain Gray, R.A.M.C., giving details of the work done at the various camps up to the 30th November last. Captain Gray has been in charge of the medical side of the scheme for the suppression of sleeping sickness since 21st May last, when Dr. Hodges, the Senior Medical Officer, went to England on leave of absence.

21. In the original project it was proposed that all persons suffering from sleeping sickness should, on removal from the lake shore, be compelled to go to one of the segregation camps, and Your Lordship will see, by a reference to paragraphs 34-38 of my despatch quoted above, the nature of the measures which we proposed to take in that connection. Dr. Hodges, however, subsequently recommended to me, very strongly, that the forcible detention of the patients in the camps should not be insisted on. He believed that any measure of rigid restraint would make the camps very unpopular, and that there would be frequent escapes. He considered it probable that the sick people would willingly come to the camps of their own accord, and that our main difficulty would be found in coping with the great numbers who would flock to us for treatment by atoxyl. It should be stated that, at that time, the reputation of the beneficial effects of atoxyl had spread through the land and that the natives were full of hope as to its results.

22. I agreed with the views expressed by Dr. Hodges. The sick have been allowed to go to the camps of their own free will, together with their relatives, and those who declined to avail themselves of our proffered help have been permitted to settle anywhere they liked provided they did not go to districts wherein the tsetse-fly might possibly exist.

23. This permissive arrangement has, I think, resulted in the treatment of a far smaller number of sick persons than we had counted on. It is already evident that the natives are losing hope as regards the results of treatment by atoxyl. The camp at Buwanuka, having been in existence far longer than any of the others, has, through its long death-roll, gained a specially sinister reputation, and there is increasing difficulty in inducing the sick to go there. Only those in a very advanced stage of the disease are taken to Buwanuka by their relatives, and the treatment by atoxyl does not, therefore, get a fair chance. The death-rate among the patients has been 26 per cent. on an average, and it is increasing. The unsophisticated natives associate the place mainly with the idea of death and shun it accordingly.

24. The other camps are much more popular but, as very advanced cases continue to be received, the death-rate is bound to increase and an unfortunate impression will probably soon be attached to them also. I hope, however, to get the chiefs to clearly explain to their people the reason for the high death-rate, and to especially impress upon them the far greater chances of recovery when the disease is treated in its early

stages. I am inclined to believe that it would be advisable to keep the patients in separate wards, according to the severity of their disease on admission. The death-rate in each section would then be instructive and would probably have some good effect on the present popular notions.

25. If the segregation of the sick be not compulsory, the success of medical efforts on an adequate scale will largely depend on the attractiveness of the camps. The funds at the disposal of the Government are so restricted that we can do no more than give a bare sufficiency of the cheapest food to the destitute patients, and as most of them belong to that class, the cost is already comparatively high. Several of the chiefs have been very generous in sending presents of milk, butter and even cattle to the camps, but these feasts are so few and far between that they are not much of an attraction. An intense craving for meat is a marked characteristic of sleeping sickness, and I think that if it were possible to give the patients a meal of beef or mutton now and then, the effect on those outside the camps would be excellent. It is possible that the sympathy of the charitable in England may be enlisted in this connection, and I propose to make an attempt in that direction.

26. It has, up to the present, not been possible to secure the required staff of hospital assistants and we have consequently had to maintain two doctors at each camp instead of one. As soon as the required men arrive, three medical officers will be freed for their proper duties, and additional camps will then be established in the hinterland of the Usoga shore and also, possibly, in Unyoro. There appear to be great difficulties in the way of establishing a camp in the island of Buvuma, and I, therefore, only propose to station a doctor there who will treat the afflicted natives at a clinique or in their own homes.

27. The supply of food to the segregation camps is becoming a matter of much difficulty, especially in the case of Buwānuka. The natives still believe sleeping sickness to be an infectious disease and are much afraid of going near the camps. The situation is being met by the creation of plantations of bananas and of sweet potatoes—the staple foods of the country—and it is hoped that, in a year's time, a sufficient supply of provisions will be available on the spot.

28. It is evident, from Captain Gray's report, that the real curative value of atoxyl in the treatment of sleeping sickness is still far from having been proved. Its effect on trypanosomes in the peripheral circulation seems to be undoubted, but it is, apparently, too early yet to judge of its permanent influence on those parasites. Dr. Van Someren reports that distressing symptoms have frequently followed the administration of the drug, and though many of the cases under treatment and observation have benefited generally to a great extent, it is by no means certain that the improvement will be permanent. It will be borne in mind that very few of the cases have been

under consecutive observation for more than a few months, and Captain Gray is of opinion that no case could be considered cured until the lapse of at least two years after the last injection of atoxyl.

29. The good and uniform quality of the atoxyl now being supplied is open to doubt, and any uncertainty on this score will, of course, seriously affect the value of all experiments that are being made with the drug. Captain Gray has drawn attention to the very large number of cases of blindness (amaurosis) which have recently occurred among patients who have been under atoxyl treatment during six months. The drug lately supplied by the manufacturers differs undoubtedly from that which was first sent out by them. It is difficult at present to say whether the blindness is a consequence to be feared from the use of atoxyl generally or whether the unfortunate cases now noted may not be due to some fault in the preparation of recent consignments of the drug. Captain Gray is making enquiry into this serious question, and the attention of the Principal Medical Officer has been drawn to it. A special report on this point will shortly be submitted to your Lordship.

30. Subject to some assurance against risk of blindness from the use of atoxyl, Captain Gray is inclined to place considerable reliance on the effect of the drug in the cases of young children in the early stages of sleeping sickness. He also suggests the compulsory removal of all infants from Buvuma. I am, however, given to understand that he has been misinformed as regards the lack of opposition, on the part of the natives, to such a project. The suggestion will not be lost sight of, and special measures for saving the lives of the little ones will have my special consideration.

31. In conclusion, I believe I am justified in saying that the measures now being taken to restrict the spread of sleeping sickness give reasonable hope of success. The tsetse on the lake-shore finds no more material to work upon; the necessary link for the transmission of the disease has been broken; and those already infected have been removed to localities where they can be of no danger to their fellow creatures. Curative measures are being tried on a large scale at various centres, and I have every reason to believe that the medical officers, entrusted with this side of the scheme, are thoroughly interested in their work and will spare no efforts to attain such success as may be possible.

32. I still believe that, with the steady continuance of consistent and strenuous efforts, sleeping sickness in Uganda will, ere long, be practically stamped out, and that the country may, at no very distant period, be freed from the terrible scourge that has swept away over 200,000 souls during the past seven years.

REPORT BY CAPTAIN A. C. H. GRAY, R.A.M.C., MEDICAL
OFFICER IN CHARGE SLEEPING SICKNESS EXTENDED
INVESTIGATIONS, ON THE SLEEPING SICKNESS CAMPS,
UGANDA, FROM DECEMBER, 1906, TO NOVEMBER, 1907.

On May 21st Dr. Hodges left Uganda on leave. Mr. Strathairn was left in charge of sleeping sickness work until I took over from him on June 18th, 1907.

Our sleeping sickness staff was still further reduced by the fact that Dr. S. Bagshawe and Dr. Wiggins had gone to England on leave and to the tragic death of Dr. Densham early in June, so that only Drs. van Someren and Uffman beside myself remained to carry on the work.

On July 4th provisional sanction to the segregation scheme arrived from the Colonial Office, and it was stated that medical officers and hospital assistants would be sent out. On August 15th final approval was given.

It was thought advisable, however, not to await the arrival of the special medical officers, but to proceed at once with the construction of further camps on the lines of that at Buwanuka, Busiro. Orders were sent at once to Dr. Baker, the Medical Officer at Jinja, to look for a suitable site for a camp in Usoga, and the Medical Officer-in-Charge left for Chagwe to select a site there.

On July 24th Dr. Baker sent word that he had found a suitable site for a camp on Bussu Hill, situated about a mile south of the Jinja-Iganga road and about two miles from Iganga. The selection of a site in Usoga presented several difficulties. Owing to the number and character of the numerous streams which pour into the Victoria Nyanza in this part of the country, tsetse fly are found much further inland in Usoga than elsewhere. It is, of course, essential that a segregation camp should be well out of fly range, but, on the other hand, our experience with the first camp at Buwanuka proved to us the unwisdom of placing a camp too far from the sleeping sickness endemic area.

The mbwa fly are also very numerous in many parts of Usoga and, except in certain areas, food has been very scanty.

However, the site at Bussu seemed eminently satisfactory and camp construction began at once, the labour being supplied by the local chiefs.

Kyetume was selected for the site of the Chagwe Camp. Kyetume lies three miles south of the Kampala-Jinja road about twenty miles from Kampala and near Mkono. Food is plentiful in this part of Chagwe, the place is easy of access, and not too far from the sleeping sickness area.

Kyetume also has the advantage of being within reach of the islands of Buvuma, where sleeping sickness is very prevalent,

and numbers of these Buvuma have already come to the camp for treatment.

The arrival of the first temporary medical officer on August 6th enabled Dr. Collyns to go to the Busiro Camp and, after learning the work, to set free Dr. van Someren. Dr. van Someren started work at the Kyetume Camp on August 19th.

GENERAL REMARKS.

Judging entirely by our first camp at Buwanuka, Busiro, which has now been in existence nearly a year, it cannot be said that a native who is suffering from sleeping sickness is very eager to present himself for treatment at such a place. The healthy native thinks that by going to a camp full of sleeping sickness patients he runs a great risk of contracting the disease himself, so that the original idea that all sleeping sickness patients should go to camp accompanied by their healthy relations who would, by their labours, provide food and necessaries for the sufferer, has not been a very popular one from the healthy relatives point of view. The result has been that a large percentage of those who have come to the Busiro Camp have been in a very advanced stage of the disease and this has necessarily meant a high death-rate, for whatever the value of medical remedies may be for a patient in a fairly early stage of sleeping sickness, it is quite certain that really advanced cases of this disease soon die in spite of medical remedies. The fact that numerous deaths occur at any camp can hardly be kept secret and the fact being known to natives who are perhaps in a quite early stage of the disease makes them unwilling to go to such a place until they feel that they have not long to live.

I do not think, however, it is quite fair to judge of the success or otherwise of future camps by our first camp at Buwanuka. Buwanuka is a long way from the sleeping sickness area (20 miles) and patients simply will not take the trouble to go there of their own accord. Among the local natives Buwanuka has also had a bad name from the violence of the thunder storms there.

DETAILED ACCOUNT OF CAMPS.

Total admission to camp up to November 30th, 1907, 1,179.

Busiro Camp, Buwanuka.

Dr. Wiggins started this camp in December, 1906, and by the time his leave was due in April, 1907, had about 300 patients under treatment. Dr. Wiggins was relieved by the late Dr. Densham early in April. On the 3rd of June news of Dr. Densham's tragic death was brought in and Dr. van Someren, who fortunately happened to be near Entebbe at the time, was at once sent to take charge of the camp. On August

19th Dr. van Someren left to start the camp for Chagwe at Kyetume and gave over charge of the Busiro Camp to Dr. Collins.

	Month.			Admissions.	Deaths.
1906—					
December	136	6
1907—					
January	71	5
February	41	10
March	78	10
April	41	16
May	32	17
June	24	15
July	28	11
August	28	9
September	16	10
October	16	16
November	14	?
Total	525	125

These patients have come from the following sazas:—

Kiadondo	... 182	Chagwe	... 74
Busiro 158	Usoga 4
Bulemezi	... 25	Unyoro	... 1
Singo 22	Buvuma	... 4
Maokota	... 21	Butembala	... 3
Busi 10	Gomba	... 2
Busuju	... 1	Bwekulas	... 1

The above figures show a more or less constant decrease in the number of admissions to the camp ever since it was first started in December, 1906.

It is a fact that this particular camp has never been popular among the natives in the country around. This fact has been brought to the notice of the Administration on several occasions, but they have been powerless to help the Medical Department in the matter. When patients, and healthy friends too, once get to the camp they are happy enough and practically never run away; they sometimes ask for a week or more's leave which is always given and in practically every case such persons return. It is obvious then that the unpopularity of this camp at Buwanuka has nothing to do with a fault in camp administration. So far, no sort of compulsion has been used in getting patients to go to our camps for treatment, and when they once get to camp no sort of measures are taken to make them stop there. It is quite certain with regard to the latter statement nothing is necessary; the camps are very popular with their actual inmates and desertions practically

never now occur. The death-rate is high from the fact that so many of the cases on admission are in an advanced stage of sleeping sickness.

In the first six months, out of 399 cases admitted to the camp, 64 had died—a death-rate of 16 per cent.

In the second six months, out of 459 cases, made up of those remaining from the previous six months and of fresh admissions, 72 died, which is also just 16 per cent.

This gives a yearly death-rate of 26 per cent.

Bussu Camp, Usoga.

On July 25th camp construction began on Bussu Hill, near Iganga. The native chiefs supplied labour very readily and a camp was soon built under Dr. Baker's supervision. Lieutenant Archibald, R.A.M.C., joined Dr. Baker on October 26th.

	Month.			Admissions.	Deaths.
	—			—	—
1907—					
August	16	—
September	47	3
October	175	18
November	90	?
				<hr/>	<hr/>
	Total to date ...			328	—
				<hr/>	<hr/>

This camp up to the present seems very popular with the Basoga. Only two patients have left since its institution. As at Buwanuka very many of the patients are in an advanced stage of the disease and will no doubt soon die.

Kyetume Camp, Chagwe.

It was not until August 21st that a medical officer was available for this camp, but Dr. van Someren, on his arrival, found that camp construction was in full swing and that patients were already there waiting for treatment. Dr. Bayon joined Dr. van Someren on his arrival in the country on October 14th.

	Month.			Admissions.	Deaths.
	—			—	—
1907—					
August	82	—
September	84	6
October	110	6
November	50	?
				<hr/>	<hr/>
	Total to date ...			326	—
				<hr/>	<hr/>

At present this camp seems very popular. A large number have come from the islands of Buvuma, where sleeping sickness is extremely prevalent. There are at the present time no less than 62 children under the age of 15 in the camp. Dr. van Someren says that, in his experience, the children make the most satisfactory progress, and that if only more of them could be got to come for treatment, our efforts to treat this disease would be more successful.

TREATMENT WITH ATOXYL, &C.

Every patient who comes to one of our camps is treated with atoxyl. An injection is given on the day of arrival and the treatment continued for from four to six months. The patients nearly always know about the treatment before they come and quite expect to be given the injections. It is only quite occasionally that any objection is offered to the treatment. In this respect the use of a fine and sharp needle to the injection syringe is important as it minimises the pain.

A freshly prepared 20 per cent. solution of atoxyl in distilled water is used. The solution must be freshly prepared, it soon turns a brown colour if kept for long and is then useless. It is also important to keep the solution in a coloured bottle.

The solution is warmed before use in order to completely dissolve the drug and to render the injection less painful. A three cubic centimetre all-glass syringe is the one generally used at our camps. The syringe is sterilised by heat and then put into weak boracic solution. No carbolic acid is used because this acid decomposes atoxyl.

The following is the method of administration:—

A spot between the patient's shoulder blades is cleaned, the needle of the syringe, which is kept lying in weak boracic solution, is then inserted well under the skin and subcutaneous tissue from above downwards. The syringe containing the measured quantity of atoxyl is then attached and the solution slowly injected. This guards against the possible breakage of the syringe from a sudden movement on the part of the patient.

METHODS OF INJECTION.

A. The original method employed. 0·4 gramme given on twentieth and twenty-first days and repeated in the same way. This method soon gave way to the next one (B).

B. The same method, but the doses given on the tenth and eleventh days.

C. Same as "B," only that the doses are increased gradually by 0·5 c.c. at a time until a maximum of 4 c.c. is reached.

D. Method recommended by Dr. van Campenhout, starting with a very small dose given and increased every five days up to a maximum of 0·7 gramme and then decreasing.

E. Method lately recommended by the German Commission, viz., one gramme (5 e.c. given on two successive days) and repeated on the fifteenth and sixteenth days.

F. Atoxyl followed by the administration of mercury by the mouth.

G. The administration of sodium-amino-phenyl-arsinate (Burroughs and Wellcome).

In addition to treatment with atoxyl, strychnine is given to any advanced cases.

The giving of mercury after atoxyl has been instituted on the advice of the Liverpool School of Tropical Medicine.

When cases of sleeping sickness arrive at our camps they are thoroughly examined by the Medical Officer-in-Charge, and, according to their symptoms, are divided into four classes as follows:—

Class A.—Those who present the following symptoms:—Fever, gland enlargement with trypanosomes present in the glands. Very often such cases complain of headache and pain in the stomach. There is no tremor. The patients on admission generally say they are well, do not think that they have sleeping sickness, or they may give a history of a few weeks' illness.

Class B.—Those presenting the following symptoms:—History of fever and some drowsiness. Think that they have got sleeping sickness; say, as a rule, that they have been ill several months. Marked gland enlargement and trypanosomes present. Impotence of some months duration as a rule or else amenorrhoea. Skin generally dry. Some slight wasting. Tremor of tongue, but not of lips or fingers.

Class C. present the following symptoms:—Well marked cases of sleeping sickness. History of illness for the last year or more as a rule. Tremor of tongue, lips, and fingers. Wasting. Dry rough skin. Generally the feet are swarming with jiggers. Such cases walk with difficulty, and are very obviously ill. They are very often either imbecile or else maniacal. Marked œdema of the lower limbs and around the eyes is often present. The lymphatic glands are enlarged and contain trypanosomes.

Class D.—Very advanced cases of sleeping sickness. Such cases are semi-comatose, and have to be carried to the camp. Are generally a mass of chiggers, and in a very filthy state. Food is only swallowed with difficulty. The mouth and lips are covered with sordes. Paralyzes are common.

It is too early yet to say very much about the value of atoxyl as a remedy for sleeping sickness. Only a few of our cases have been under observation for as long as 12 months. In the following table the after history of those cases admitted to our Busiro Camp up to August 1st is tabulated.

Only undoubted cases of sleeping sickness are included in this table, and all cases who have died of some intercurrent disease, or have run away, are excluded. The admissions for each month are kept separate for the reason that a case admitted in December, 1906, or January, 1907, has been under observation so many months longer than subsequent admissions.

All cases in this table have undergone a course of atoxyl treatment for at least four months. Methods A., B., C., and D. have been those generally employed. (*See above for methods of giving atoxyl.*)

Cases Admitted in December, 1906.

Present State, November 30th, 1907.	Class of Case on Admission.				Totals.
	Class A. 33 Cases.	Class B. 51 Cases.	Class C. 30 Cases.	Class D. 9 Cases.	
Showing improvement after a course of atoxyl. Not now taking the drug.	16	24	4	—	44
Continue to take atoxyl. No marked improvement.	—	6	3	—	9
Relapsed after temporary improvement. Atoxyl resumed.	13	10	3	—	26
Died after a course of atoxyl	4	11	20	9	44
Total admissions treated	123

Cases Admitted in January, 1907.

Present State, November 30th, 1907.	Class of Case on Admission.				Totals.
	A. 8.	B. 25.	C. 25.	D. 4.	
Showing improvement after a course of atoxyl. Not now taking the drug.	6	13	1	—	20
Continue to take atoxyl. No marked improvement.	—	4	1	—	5
Relapsed after temporary improvement. Atoxyl resumed.	1	4	—	—	5
Died after a course of atoxyl	1	4	23	4	32
Total admissions treated	62

Cases Admitted in February, 1907.

Present State, November 30th, 1907.	Class of Case on Admission.				Totals.
	A. 13.	B. 14.	C. 10.	D. —.	
Showing improvement after a course of atoxyl. Not now taking the drug.	10	6	1	—	17
Continue to take atoxyl. No marked improvement.	3	1	2	—	6
Relapsed after temporary improvement. Atoxyl resumed.	—	4	2	—	6
Died after a course of atoxyl	—	3	5	—	8
Total admissions treated	37

Cases Admitted in March, 1907.

Present State, November 30th, 1907.	Class of Case on Admission.				Totals.
	A. 9.	B. 39.	C. 23.	D. 1.	
Showing improvement after a course of atoxyl. Not now taking the drug.	5	15	1	—	21
Continue to take atoxyl. No marked improvement.	3	7	—	—	10
Relapsed after temporary improvement. Atoxyl resumed.	1	10	2	—	13
Died after a course of atoxyl	—	7	20	1	28
Total admissions treated	72

Cases Admitted in April, 1907.

Present State, November 30th, 1907.	Class of Case on Admission.				Totals.
	A. 2.	B. 28.	C. 9.	D. 2.	
Showing improvement after a course of atoxyl. Not now taking drug.	2	13	3	—	18
Continue to take atoxyl. No marked improvement.	—	—	—	—	—
Relapsed after temporary improvement. Atoxyl resumed.	—	10	2	—	12
Died after a course of atoxyl	—	5	4	2	11
Total admissions treated	41

Cases Admitted in May, 1907.

Present State, November 30th, 1907.	Class of Case on Admission.				Totals.
	A. —.	B. 20.	C. 12.	D. —.	
Showing improvement after a course of atoxyl. Not now taking drug.	—	11	2	—	13
Continue to take atoxyl. No marked improvement.	—	4	1	—	5
Relapsed after temporary improvement. Atoxyl resumed.	—	1	—	—	1
Died after a course of atoxyl	—	4	9	—	13
Total admissions treated	32

Cases Admitted in June, 1907.

Present State, 30th November, 1907.	Class of Case on Admission.				Totals.
	A. 4.	B. 13.	C. 7.	D. —.	
Showing improvement after a course of atoxyl. Not now taking the drug.	3	13	3	—	19
Continue to take atoxyl. No marked improvement.	—	—	2	—	2
Relapsed after temporary improvement. Atoxyl resumed.	1	—	—	—	1
Died after a course of atoxyl	—	—	2	—	2
Total admissions treated	24

Cases Admitted in July, 1907.

Present State, 30th November, 1907.	Class of Case on Admission.				Totals.
	A. 5.	B. 7.	C. 14.	D. —.	
Showing improvement after a course of atoxyl. Not now taking the drug.	4	4	7	—	15
Continue to take atoxyl. No marked improvement.	1	3	7	—	11
Relapsed after temporary improvement. Atoxyl resumed.	—	—	—	—	—
Died after a course of atoxyl	—	—	—	—	—
Total admissions treated	26

The above tables of cases admitted to Busiro Camp during the period December, 1906, to July 31st, 1907, bring out the following points:—

That the deaths which occur month by month at this camp, occur chiefly among those patients who have been in the camp a long while, and that comparatively few new arrivals die until they have been in the camp three or four months, and have had a course of atoxyl.

We see from the above tables that in spite of a course of atoxyl—

Of the December cases 36 per cent. are dead by November 30th, 1907.

Of the January cases 51 per cent. are dead by November 30th, 1907.

Of the February cases 21 per cent. are dead by November 30th, 1907.

Of the March cases 39 per cent. are dead by November 30th, 1907.

Of the April cases 26 per cent. are dead by November 30th, 1907.

Of the May cases 40 per cent. are dead by November 30th, 1907.

Of the June cases 8 per cent. are dead by November 30th, 1907.

Of the July cases none are dead by November 30th, 1907.

Of cases admitted in August, September, October, and November, in all six are dead, five of whom were brought to camp in a dying condition.

These facts seem to show that atoxyl has a temporary good effect on sleeping sickness patients, but that this effect in the great majority of cases is only a temporary one, as nearly half the cases admitted in December, 1906, and January, 1907, are now dead.

It will be seen from the above tables also, that in 231 cases atoxyl was remitted. These cases were selected because they presented the following features:—

There was an absence of trypanosomes from the glands, and the patients appeared well and fairly strong. A few of them presented tremor of the tongue and itchiness of the skin, but they had all been under atoxyl treatment for at least four months, the majority for six months. Sixty-four of these cases have relapsed up to the present. (Note: that there generally was an interval of some three or four months, during which time the patients were having no atoxyl, before the relapse became evident.) Twenty-eight of these people in whom atoxyl was remitted as above have died up to the present (November 30th, 1907).

Dr. van Someren, reporting on the value of atoxyl treatment, in August says:—

Up to the present I have never seen any untoward symptoms follow the injection of one gramme atoxyl. Injections are sometimes followed by a slight rise of temperature, and by some pain in the chest, which, however, soon disappears. There have been 95 deaths up to the present time in the camp, of these five died from extraneous causes; 27 died fairly soon after admission, having had only a few injections of atoxyl; the remaining 63 showed a marked initial improvement, but subsequently died after a shorter or longer interval. This may seem a large number, but it must be borne in mind that many of the patients were brought in in a very late stage of the disease. Epileptiform seizures towards the end were very common. In some cases these seizures recurred rapidly, and were prolonged in duration. A sudden access of mania, terminating fatally in a few days, occurred in one case that had been under treatment for eight months.

Various paralyses, both hemiplegic and paraplegic in type, were present, a glosso-pharyngeal type being common, the patient, though appearing from his expression to be mentally bright, being unable to speak or swallow. Bed-sores in the paralytic cases were, as to be expected, distressingly common, and often reached great dimensions.

It is evident from these that in certain cases the drug proves quite ineffectual in arresting the disease. This leads one to suspect that though temporarily checked, the trypanosome subsequently acquires an immunity to this drug. Initial large doses, given consecutively, might, therefore, be of value.

In no case have trypanosomes been found after the treatment with atoxyl in the superficial lymphatic glands, the earliest disappearance of the parasite being in our experience about 12 hours after the first dose with the non-appearance at any subsequent period as far as can be made out. A certain number of cases, however, while appearing outwardly healthy, and even the patient himself may declare that he feels well, yet, on examination, one finds that they have a continuous irregular temperature, rising possibly to 103° F. or more every evening with remissions to normal or subnormal at intervals, but in the main fluctuating between normal and 100° F. By special request of His Excellency the Governor, no lumbar punctures or post-mortem examinations are performed at our camps for fear of rendering them unpopular, so that it is impossible to say more than that after atoxyl, the trypanosomes cannot be found in the blood or gland juice. It may be that trypanosomes could be found in the cerebro-spinal fluid, in fact, this was actually found to be the case by Dr. Collens in a patient who had undergone a course of atoxyl, and in whom a continuous temperature persisted, though trypanosomes could not be found in the glands or blood.

Trypanosomes have not reappeared in the blood or lymphatic glands of any of these cases up to the present. In most cases the formerly enlarged lymphatic glands have decreased in size to a remarkable degree, and in many no gland enlargement can now be recognised.

Loss of sexual power is a very common and early symptom of sleeping sickness; the sexual history of 75 people is as follows:—

29 of them have regained their sexual functions after a cessation of from four months to two years in some cases.

15 patients, though feeling otherwise sound, are still either impotent or amenorrhœic.

31 cases, including children, have been sexually normal throughout the course of the disease.

These facts seem to show that in some cases this drug is of very real benefit.

Up to September, 1907, Dr. van Someren says concerning atoxyl "In no case as yet has any untoward symptom occurred which could be attributed to any toxic effects from the drug. I have had several cases of intense vertigo, which I thought at first might be due to an excessive dose or to an accumulative effect of the drug, but vertigo I found to be a fairly common symptom in fresh cases, and further, there appeared to be no difference in the duration of the attack, whether the drug was intermitted or not. The administration of 5 c.c (one gramme) of atoxyl to an adult is followed by absolutely no reaction beyond, in some cases, a slight rise of temperature subsequently, such as is often met with."

Father Vurangot, of the "White Fathers," reporting at the middle of August on his experience with atoxyl and on its value says: "I have been giving atoxyl in doses of 5 c.c of a 20 per cent. solution (one gramme) repeated every nineteenth or twentieth day. I have treated four cases in this way for as long as nine months. I think three of these four are now cured of the disease.* I have never seen a dose of atoxyl followed by urgent symptoms, but some of the patients to whom I have given injections have had high fever for one or two days afterwards, which has abated without the use of quinine. Equally the majority of those who have had atoxyl have complained of pain in the chest afterwards, but this symptom only lasts for two or three days. I have never seen an abscess follow on an injection of atoxyl."

I take it that this must also be the opinion of the German Commission under Professor R. Koch, who left Sese at the beginning of October of the present year, for Professor Klein, before he left Uganda, advocated the giving of atoxyl in doses of one gramme on two consecutive days, and repeating the same in a fortnight's time.

* I have personally examined these cases. Trypanosomes cannot be found in their glands or blood and they seem at present normal individuals.

Dr. van Someren, reporting again on atoxyl on October 29th, said that he had had a succession of patients with symptoms which he thought were undoubtedly due to the toxic effects of arsenic. That he had been giving atoxyl in exactly the same doses as usual, and that further, the toxic symptoms had manifested themselves after comparatively small doses in cases who had not been treated before. Dr. van Someren then gives details of 19 cases, all of whom developed more or less urgent symptoms within 48 hours of their injections, such as intense colic, vomiting, vertigo, and intense headache. Five patients developed amaurosis. He goes on to say that luckily he had no fatal cases in which blame could be laid on the drug, and that he had been able to allay the distress fairly quickly in most of the sufferers.

Dr. van Someren adds that this uncertainty in the action of our present supply of atoxyl renders the estimation of the doses for any particular patient much more difficult than formerly.

On receipt of this communication from Dr. van Someren I immediately sent word to Drs. Baker and Collyns, who are in charge of our camps in Usoga and Busiro, to report on their experience with this atoxyl. Both these doctors reported that they had noticed differences in the atoxyl that had recently been supplied to them.

- (1) It was much more soluble than former samples.
- (2) The solution of the drug changed colour much sooner than formerly (more unstable).
- (3) That its administration did not seem to be followed by the same improvement in their patients which had been previously noted with former samples of the drug.
- (4) That, however, they had not found that urgent symptoms followed its administration.

Amaurosis has been noted 14 times at Busiro—always in people who have been on atoxyl a long while, and Dr. van Someren reports five more cases, which he puts down to the new supply of atoxyl. As these cases all seemed to come together, it is certainly very suspicious. Up to the time of Dr. van Someren's report, the medical officer in charge at Busiro had not connected the cases of amaurosis that had occurred there as due to the atoxyl. I am not aware that amaurosis has ever been mentioned as a symptom of sleeping sickness by any observer before, whereas I believe it has been reported before, after injections of atoxyl, and may be due to the aniline which it contains.

To get the greatest value from atoxyl treatment, it seems that the initial doses of the drug should be as large as possible. Recent work on the subject seems to show that in some cases

the trypanosomes become accustomed to the drug and unaffected by subsequent doses. The uncertainty of the action of our present supply of atoxyl, however, very naturally makes our medical officers chary about using it in large doses.

The administration of atoxyl combined with strychnine and judicious feeding has been attended over and over again with most astonishing results. Patients, who on admission have seem moribund, have several times been up and walking in a few days. This improvement is, unfortunately, only temporary, and no doubt the better feeding and the strychnine have much to do with it.

ATOXYL FOLLOWED BY MERCURY.

It is only lately that this treatment has been instituted, and it is, of course, too early to judge of results.

The native, as a rule, stands mercury badly by the mouth.

On the suggestion of Colonel Lambkin, Royal Army Medical Corps, we shall try the administration of metallic mercury following on a course of atoxyl as soon as ever this special preparation can be obtained.

SODIUM-AMINO-PHENYL—ARSINATE. (Burroughs and Wellcome.)

A small supply of this drug, sent to us by the makers, has been tried by Dr. van Someren, who reports favourably upon it, and says that trypanosomes have not yet returned to the glands of those few people to whom he has administered it, and that it seems as good as atoxyl. A further supply has been sent for from the makers. As this preparation is only half the price of atoxyl, it is certainly worth a more extended trial, especially as there seems to be a good deal of uncertainty in the action of our present supply of the latter.

LUNATICS.

As sleeping sickness is accompanied by grave pathological changes in the brain and nervous system, it is not surprising that many patients suffer from attacks of mania.

The average advanced case is a harmless imbecile, but violent mania is sometimes seen. Sixty-one patients in all have had to be isolated and restrained in our various camps. Each of our camps is now provided with a special lunatic annexe to which violent cases can be sent. Our camp buildings are, of course, only roofed with dried grass; on two occasions lunatics have succeeded in setting fire to the camps, and have done a great deal of damage. Native warders are in charge of them both day and night. Violent patients are handcuffed, but

there is always the danger that some patient may become suddenly maniacal, and burn down the whole camp.

On the whole treatment has been very successful with these maniacal patients, and prolonged restraint is hardly ever necessary.

All our medical officers report on the frequency of epileptiform fits. Patients soon die after these fits have once commenced.

SMALL-POX.

Small-pox being common in so many parts of Uganda, and the natives being practically unprotected by vaccination, it is surprising that so few cases have occurred in our camps. A bad case of confluent small-pox occurred at Kyetume Camp, in Kyagwe, but prompt measures of isolation were taken, and vaccine lymph telegraphed for at once from the Government vaccine farm, Nairobi, and obtained in four days, so that an outbreak was avoided. Vaccine lymph cannot be kept at a camp in good condition owing to the absence of ice.

CHIGGERS.

Chiggers are the pests of our camps. Every advanced case of sleeping sickness that is admitted swarms with them, and they multiply with fearful rapidity. In a bad case of sleeping sickness, the chiggers are not confined to the feet; the hands are often a mass of them, mouth, nose and ears get infected in turn, and the result is a truly revolting spectacle.

A special large hut has been built, to which all cases go once a week, and their chiggers are there removed by native attendants, four of whom at each camp are kept constantly employed doing nothing else. By the use of large quantities of "Jeyes fluid," and by constant sweeping, these parasites are kept in some sort of check.

LICE.

Lice are also very common, and to preserve anything like cleanliness a large staff of native attendants is essential. The average native is quite convinced that sleeping sickness is a contagious disease, and it is difficult to get the attendants to do much for the very sick. This difficulty has been partly got over by employing as hospital attendants patients in an early stage of the disease. Towards the end, as the bladder and rectum become paralysed, bed-sores are the rule. When coma sets in, the patients are removed from the wards, and put into separate huts or compartments of a large hut. This is done in order that the other patients in the ward may not be constantly confronted by the dying, and for the sake of general hygiene. The small huts can be afterwards destroyed and new ones built at a trifling cost.

FOOD SUPPLY.

An unfortunate drought has made the problem of keeping our camps properly supplied with food sometimes a difficult one. Clearing and planting is going forward now that the rains have started, but it will be sometime before any camp will be able to supply its own needs. The Muganda prefers bananas to anything else and it takes more than a year to get a satisfactory crop, counting the time spent in first clearing the ground. Sweet potatoes give a crop in four months and these are being planted as fast as possible; they have the additional advantage of requiring practically no attention when once the cuttings have taken root. Banana suckers are also being planted, but not to the same extent as potatoes, the former require more or less constant attention, the labours of one individual being only sufficient to supply himself and two others with this food. A new camp must therefore depend on outside sources for its food supply for many months. We have had to employ outside labour to a large extent for our clearing and planting. Many of the patients are quite capable of doing a little work, but they generally refuse, their excuse is that they are going to die and that they are not going to plant food for others to eat. A certain amount of work has been done by healthy relations who have accompanied patients to camp, but the presence of such relatives is the exception rather than the rule, the latter much preferring to just leave the sick one and then disappear as fast as possible.

Patients, when they first come to camp, generally have a little money, but this is soon exhausted and then they have to be fed at Government expense. The knowledge that free food can be obtained at our camps generally makes patients on their arrival represent themselves as destitute, even if they have a little money, and it is practically impossible to prove the truth of their statements. A suggestion has been made to the native parliament that all patients coming to camps for treatment should bring a letter from their local chief stating whether the bearer is actually destitute or otherwise, but nothing has so far come of this. It will not be long before every patient in our camp will have to be fed at Government expense. The present cost to the Government of buying food works out at one shilling per head per month, this, however, does not include the cost of bringing the food to the camp. Labour for this is supplied by the local chiefs and food often has to be brought long distances; this is especially the case at our camp at Busiro which has already consumed all the food in its immediate neighbourhood.

A native bed, barkcloths, cooking pots, and sometimes a blanket have also to be provided for a destitute patient.

Meat in small quantities, milk and native butter are provided for the very sick, which are either bought by Government

or else presented by the chiefs who have on many occasions been very generous in this respect. One bullock a month in addition is killed at each camp. The native is very fond of meat, and it was hoped that this would help to attract patients for treatment. A certain number of people come to our camps representing themselves as having sleeping sickness or who have been so informed by relatives or others who do not want the trouble of looking after them, when they have not really got sleeping sickness or any symptoms of it. As a rule, these people are old and past work or else suffering from some disease other than sleeping sickness, and, in any case, are a burden to themselves and their relatives and they have heard or been told that they will be given food at our camps. It is with great difficulty that some of these people are got rid of.

The various missions have taken a great interest in our camps. Chapels of both denominations have been built at Buwanuka and are going to be built at Kyetume. Our Usoga camp is close to a mission centre. The camps are constantly visited by missionaries and native teachers. The natives appreciate this and it all helps towards the main object—to make our camps attractive.

Our camps in Kyagwe and Usoga seem to be very popular as the present rate of admission shows.

On November 26th Dr. J. H. Goodliffe departed for the Sese Islands to start a camp on the main island (Bugalla) close to that lately vacated by the German Commission under Professor R. Koch. Many patients have already been treated with atoxyl on these islands. Dr. Goodliffe, in his first letter to me, says that the people, though pleased to have a doctor among them, do not seem very anxious for further atoxyl treatment and thinks they are disappointed with what they have already seen of it.

The islands of Buvuma are still a centre of sleeping sickness. A few patients are going to Kyetume, the nearest camp. Dr. van Someren, after a recent visit to the island, says that he saw a great number of sick, but only a very small percentage of the total number. The chiefs on the island said that they were having the greatest difficulty in getting the people to go across to Kyagwe, as they did not know Uganda and had all sorts of curious ideas about our camps there. He says that such of the Buvuma who have come to camp have very soon got over their terror, that some have gone on a visit to their homes and have returned to camp again bringing others with them. Dr. van Someren goes on to say, "from what I can gather as to the customs of the islanders it will be almost, if not quite, an impossibility to expect to form camps, such as we have in Uganda, on Buvuma Island, owing to the inadequate food resources, and when it is borne in mind what a great source of infection the islands are, it seems a pity that these persons are

not removed as far as possible for a time at least, as it seems reasonable to hope that in time the infection will die out from the fly when the reservoirs of the trypanosomes are removed." I would like to draw attention to this, owing to the large number of children, relatively, that from Buvuma, every one of them is infected. I may say that practically every Muvuma who has come under my notice has been infected, in many cases I have been able to find the trypanosomes in those who declare that they are perfectly well, and I am inclined to the belief that if a systematic examination was made of the inhabitants of these islands, the percentage of infected persons would be found to be 95 per cent. if not more. The estimated population of these islands at the present time is 6,000. I do not think that a general order to have at least all the children brought for treatment would meet with any great objection, since so many of them are orphans, nor would those who might come over without their parents feel strange for more than a little while, seeing that little home life, as we understand it, there is amongst them.

In conclusion, may I be allowed to point out that our doctors who are in charge of these camps are considerably handicapped by the absence of any proper "Hospital Assistants." So far natives have been the only assistants available, with the result that all clerical work, as well as medical, has fallen on the shoulders of medical officers.

Disputes and petty offences are common among the patients, and these are always brought to the medical officer to settle as being the only white man there. In addition the medical officer has to superintend all the planting and clearing that is going on. The presence of so many lunatics and the chance that some one may set fire to the hospital buildings, makes it almost impossible for the medical officers to leave their camps for even an hour at a time.

Entebbe,

December 6, 1907.

FURTHER REPORT ON THE MEDICAL TREATMENT OF SLEEPING SICKNESS PATIENTS AT THE SEGREGATION CAMPS, January 18th, 1908. BY CAPTAIN A. C. H. GRAY, R.A.M.C.

In the report which I submitted on December 12th, 1907, I described the methods of treatment in use at our camps, and said that I was preparing some further details about atoxyl treatment.

It is now one year since the first of the segregation camps was started at Buwanuka, Busiro, so that the facts in this report cover a period from December 1st, 1906—November 30th, 1907.

During this period the following number of patients have received treatment:—

During the first quarter (December 1st, 1906—February 28th, 1907)	222
During the second quarter (March 1st— May 31st)	145
During the third quarter (June 1st—August 31st)	172
During the fourth quarter (September 1st— November 30th)	596
A total number of patients	<hr/> 1,135 <hr/>

Of these 1,135 cases of sleeping sickness, the medical officers in charge of the camps report on November 30th, 1907, that—

517, or 45 per cent., have definitely improved under treatment, and that this improvement has, up to the present, been maintained.

77, or 7 per cent., have relapsed after a temporary improvement, but are still alive.

284, or 25 per cent., continue in the same state as they were on admission.

220, or 19 per cent., are dead.

37, or 4 per cent., were away at the time of this examination.

As I said in my previous report, all sleeping sickness patients on arrival at camps are noted down by the medical officer in charge as belonging to one of four classes by the symptoms that they present. Cases are either—

A. Very early cases, who feel, as a rule, well and strong, but present the signs of gland enlargement and the symptoms of occasional attacks of fever and headache.

140 of such cases have been admitted.

B. Early cases, who present symptoms such as itchy skin, pain in the legs, tongue tremor, impotence or amenorrhœa, but who are mentally normal though there may be fits of drowsiness.

493 of such cases have been admitted.

C. Advanced cases, who are mentally slow, dull, and expressionless. There is commonly tremor of the tongue, lips, and fingers. Such cases generally walk with difficulty, and are very obviously ill. Some wasting of the body is very commonly present.

431 of such cases have been admitted.

D. Very advanced cases are drowsy, bed-ridden, swallow food with difficulty, and are generally much emaciated. Chiggers are very numerous, and bed sores common.

71 of such cases had been admitted.

If we examine the after history of these cases class by class, we find that—

Of 140 A cases—

88 have improved, and the improvement has been maintained.

16 have relapsed after temporary improvement.

18 continue in the same state.

5 have died.

13 absent at the time of examination, but living.

Of 493 B cases—

266 have improved as above.

44 have relapsed.

126 continue in the same state.

44 have died.

13 were absent at time of examination, but living.

Of 431 C cases—

156 have improved.

14 have relapsed.

134 continue in the same state.

116 have died.

11 were absent at time of examination.

Of 71 D cases—

7 have improved.

3 have relapsed.

6 continue in the same state.

55 have died.

If the A and B cases are grouped together as early cases, and the C and D cases as late cases, the comparison works out as follows:—

Present State on November 30th, 1907.	Early cases.	Late cases.
	Per cent.	Per cent.
Improved	56	32.5
Relapsed after temporary improvement ...	9	3.5
Continue in the same state	23	28
Died	8	34
Absent at the time of examination ...	4	2

The following four tables show the present condition of patients admitted during the four different quarters of the year, and the fifth is a comparison of the other four.

TABLE Showing the Present State of the Admissions between December 1st and February 28th (first quarter)

Present State on November 30th, 1907.	Class of Case on Admission.				Totals.
	A.	B.	C.	D.	
Improved	32	43	6	—	81
Relapsed, after temporary improvement.	14	18	5	—	37
Continue in the same state	3	11	6	—	20
Died	5	18	48	13	84

Total quarter's admissions treated 222

TABLE Showing the Present State of Admissions between March 1st—May 31st (second quarter).

Present State on November 30th, 1907.	Class of Case on Admission.				Totals.
	A.	B.	C.	D.	
Improved	7	39	6	—	52
Relapsed, after temporary improvement.	1	21	4	—	26
Continue in the same state	3	11	1	—	15
Died	—	16	33	3	52

Total quarter's admissions treated 145

TABLE Showing the Present State of the Admissions between June 1st—August 31st (third quarter).

Present State on November 30th, 1907.	Class of Case on Admission.				Totals.
	A.	B.	C.	D.	
Improved	16	52	33	2	103
Relapsed after temporary improvement.	1	5	2	1	9
Continue in the same state	1	19	21	—	41
Died	—	2	5	9	16
Absent at time of Examination.	2	1	—	—	3

Total quarter's admissions treated 172

TABLE Showing the Present State of the Admissions between September 1st—November 30th (fourth quarter).

Present State on November 30th, 1907.	Class of Case on Admission.				Totals.
	A.	B.	C.	D.	
Improved	33	132	111	5	281
Relapsed after temporary improvement.	—	—	3	2	5
Continue in the same ...	11	85	106	6	208
Died	—	8	30	30	68
Absent at time of Examination.	11	12	11	—	34

Total quarter's admissions treated 596

TABLE Comparing the Present State of Patients Admitted During the Different Quarters of the Year.

Present State on November 30th, 1907.	Admissions during the—			
	First Quarter.	Second Quarter.	Third Quarter.	Fourth Quarter.
	Per cent.	Per cent.	Per cent.	Per cent.
Improved	37	36	59	47
Relapsed after temporary Improvement.	16	18	5	1
Continue in the same state ...	9	10	24	35
Died	38	36	10	11
Alive but absent at the time of examination.	—	—	2	6

METHODS OF TREATMENT USED.

The great majority of our cases have, up to the present, been treated entirely with atoxyl combined with strychnine (in the case of patients in an advanced state of the disease).

The methods of atoxyl treatment employed, as I stated in my previous report, have been:—

(a.) The original method employed: 0·4 gramme given on the twentieth and twenty-first days, and repeated for an indefinite period. This method was soon discarded for:—

(b.) Similar to the above, but the injections are given on the tenth and eleventh days.

(c.) Similar to the above (b), but the doses are gradually increased by 0·5 c.c. at a time until a maximum of 0·7 gramme is reached. This is continued for a month, and then the dose reduced.

(d.) Dr. van Campenhout's method—very similar to method (c), except that the initial dose is much smaller, the injections are given every fifth day up to a maximum of 0·7 gramme, and continued at this point for a month.

(e.) Method lately recommended to us by the German Commission. One gramme of atoxyl on two successive days, and repeated on the fifteenth and sixteenth day.

Our medical officers have used method (b) as a routine method.

When there is only one medical man at a camp to attend to four or five hundred patients, a method which entails as few injections as possible during a month is a great advantage. Method (e), which entails only four injections in a month, would, therefore, seem useful, but the doses are large, and as there has been some reported uncertainty in the action of some of the atoxyl supplied to us, it has only been used in a few cases. The actual results that we have obtained with atoxyl alone are shown in this table:—

CASES TREATED WITH ATOXYL ALONE.

779 Cases.

Present State on November 30th, 1907.	One Month's Treatment.		Two Months' Treatment.		Three Months' Treatment.		Totals.
	Amount of Atoxyl given in Grammes.						
	Under 2 Grms.	2-4 Grms.	4-6 Grms.	6-8 Grms.	8-10 Grms.	Over 10 Grms.	
Improved	—	38	107	84	32	64	325
Relapsed after im- provement.	—	4	10	22	10	18	64
Continue in same state.	8	51	44	15	21	51	190
Died	66	44	34	21	14	21	200
Total	74	137	195	142	77	154	779

211 cases treated for one month.

337 „ „ „ two months.

231 „ „ „ three months.

And the following table gives a comparison of the results obtained in patients who have been treated for one, two, and three months consecutively:—

Present State, November 30th, 1907.	Duration of Treatment.		
	One Month.	Two Months.	Three Months.
Improved	19 per cent.	56·5 per cent.	41 per cent.
Relapsed	2 "	9·5 "	12 "
Continue in same state ...	29 "	18 "	31 "
Died	50 "	16 "	16 "
Number of cases	211	337	231

The high death-rate among cases treated for one month in the above table is due to the fact that lately we have had a large number of patients in a state of starvation in Usoga, who have only lived long enough to receive a month's treatment in camp.

A point that the above table seems to show is that rather fewer cases show improvement after three months' atoxyl treatment than after two months' treatment (41 per cent. of the former against 56·5 per cent. of the latter), the percentage of deaths in the two cases being the same.

As I mentioned in my previous report, there seems to be no doubt at all that more than half the cases of sleeping sickness show marked temporary improvement in their general bodily health after atoxyl treatment, and the enlarged glands diminish rapidly in size in nearly every case.

Up to the present our Medical Officers have only twice succeeded in finding trypanosomes in patients who are at the time actually undergoing a course of atoxyl treatment—once in the gland juice and once in the blood, and only twice in patients who have left off atoxyl. However, as can be seen from these tables, even in the case of early cases of this disease who have been under observation one year, taking the A and B cases admitted during the first quarter—75 in number—that 23 of them (or 34 per cent.) are dead at the end of the year.

Owing to the fact that our medical officers have had no trained hospital assistants to help them they have not had the time to thoroughly examine the treated cases for trypanosomes.

The gland juice of these cases has been examined, and the medical officers are unanimous in reporting that hardly ever can trypanosomes be found there after treatment, and that in the majority of patients the gland enlargement disappears. The period since the last dose of atoxyl was given has, however, not been more than a few months in the case of these treated cases, and it may be that trypanosomes will yet re-appear in a

good many. This absence of trypanosomes from the lymphatic glands cannot mean that all the trypanosomes throughout the body have been destroyed in these people, because, as I have just said, 34 per cent. of the early cases (A and B cases) that have been under continued observation for a year are dead at the end of that period in spite of the fact that the gland juice does not contain parasites. When our medical officers have more time to make exhaustive examinations of the blood and cerebro-spinal-fluid of treated cases, I cannot help thinking that trypanosomes will be found in a great many.

With regard to treatment by other methods, the following table shows that 294 people have been treated with atoxyl combined with mercury.

The method employed up to the present consists of giving two injections of 0.4 gramme of atoxyl on two successive days followed by one-sixth of a grain of perchloride of mercury given hypodermically after an interval of three days, and this latter injection repeated three or four times at a three days' interval unless untoward symptoms manifest themselves. A few cases who did not look after their mouths properly did complain of sore gums as a result of these injections of mercury, but in the rest no bad result was followed.

It is only three months since this treatment was started by Dr. van Someren, and the results have been encouraging as seen by the table.

TABLE showing the number and present condition of patients treated with atoxyl and mercury (hypodermic injections) and mercury alone (intravenous injections).

Present State, November 30th, 1907.	Atoxyl and Mercury.	Mercury alone.
Improved	183	—
Relapsed after course of treatment ...	1	—
Continue in the same state	90	3
Died	20	—
Totals treated	294	3

Three cases have been treated by means of intravenous injections of a mercury salt by Dr. Bayon, but without any marked improvement following.

We have not had sufficient sodium-amino-phenyl-arsinate (Burroughs and Wellcome) to give it a proper trial, but a consignment of the drug has just arrived, and a certain number of patients will be systematically treated with it.

In a certain number of cases, patients who have been treated with atoxyl have developed symptoms suggestive of intoxication.

These cases are given in detail in the accompanying table, which shows the amount of atoxyl received by each case before the symptoms described were noticed.

Giddiness has been by far the commonest symptom complained of. It is true that a certain number of people complain of this symptom on admission before any treatment has been started, but still the large number of cases that have complained of this symptom (10 per cent. of the whole) of late makes me think that in many it is due to the atoxyl. I may say that this opinion is not held by all our medical officers, some of whom look on it entirely as a symptom of sleeping sickness.

Colic and diarrhœa noted in four per cent. of treated cases. Has come on generally within twelve, or at most twenty-four, hours of an injection of atoxyl. In four cases it has been of a severe type.

Alteration of the vision has been noticed in forty-seven cases. In thirty-three it has taken the form of dimness of vision. Of these 33 cases—

In 12 the visual dimness has improved.

5 remain in the same condition, getting neither worse nor better.

2 have died with the symptoms as above.

14 have got worse.

Four of these cases had marked dimness of vision on admission before any atoxyl had been given them, but still I think that in most of the cases, the atoxyl has been the cause.

It is a suspicious fact that except in these four cases the condition was not noticed in Busiro Camp until September, 1907. The great majority of the people who have suffered in this way, have been treated by a system of atoxyl injections entailing a slightly increased dose at each set of injections though in no case has a dose larger than 0·7 gramme been given at one time. Most of the cases in whom it has been noticed were well marked cases of sleeping sickness on admission to camp.

It is curious that only one case had been reported from the Usoga Camp, and yet Dr. Baker, the Medical Officer in Charge, has been treating a certain number of cases there with gramme doses of atoxyl.

Fourteen patients have become totally blind (1·2 per cent. of the whole). The details of these cases I give in a special table as the symptom is such an important and distressing one.

It will be noticed from the table that eleven of these cases have been treated with increasing doses of atoxyl. That in no case had the dose exceeded 0·7 gramme at a time, that the average period of treatment for each case so afflicted works out

at 3½ months, and the average total amount of atoxyl taken by each at eight grammes during that period. Three of these people were never given a larger dose than 0·4 gramme. That half the cases belonged to class B and half to class C on admission. Blindness is described as a symptom of aniline poisoning. A certain amount of the atoxyl supplied to us, as I mentioned in my previous report, was of a light yellow colour, in powder, and made up into a yellow solution immediately it was prepared. This yellowness was, I think, due to free aniline. The cases of dimness of vision and blindness which have occurred have all been noticed with one exception since August 1st, and it was at just this time that this yellow atoxyl was being used by our medical officers. I think this symptom may be due to aniline poisoning.

Ophthalmoscopic examination of these cases has generally proved negative.

Paresis of lower limbs with increased knee jerk is generally looked upon by our medical officers as a symptom of sleeping sickness. Dr. Collyns, however, is of opinion that it may have been due to the atoxyl in twelve cases.

Sudden death.—Seven patients have died suddenly for no very apparent reason within forty-eight hours of atoxyl injection. *Post-mortem* examinations are not allowed at our camps because of the fear that they would thereby be rendered unpopular. I do not for a moment say that these deaths have been caused by the atoxyl, but the fact is serious, and ought to be noticed.

Two other symptoms have been commonly noticed after atoxyl injections—præcordial distress, and a rise of temperature. Both these symptoms soon disappear. Aniline is said to cause the formation of methæmoglobin in the blood. Perhaps the præcordial distress may be accounted for in this way.

All our medical officers are of the opinion that, provided that the quality of the atoxyl is above suspicion, the good results in the way of marked temporary improvement in the general health, and the fact that patients are rendered innocuous, and that perhaps cures may be obtained by its administration out-weigh any bad results that may possibly occur through its use, and that until a better substance can be found, we are justified in going on with the treatment.

APPENDIX.

TABLE showing the number of sleeping sickness patients who presented certain symptoms possibly due to the atoxyl administered to them, showing the amount of atoxyl taken in each case before such symptoms were noticed.

Character of Symptoms Observed.	Amount of Atoxyl Taken—in Grammes.						Totals.
	Under 2.	2-4.	4-6	6-8.	8-10.	Over 10.	
Marked giddiness ...	10	35	34	19	2	—	100
Colic and diarrhœa, often with vomiting.	16	16	6	4	—	—	42
Alteration of vision ...	1	2	7	13	3	7	33
Total blindness ...	—	—	5	3	3	3	14
Paresis of lower extremities with increased knee jerks.	—	2	—	3	2	5	12
Sudden death with no apparent cause.	7	—	—	—	—	—	7
Vomiting only ...	1	—	—	—	—	—	1

TABLE showing number of patients, type of case on admission, sex, system of treatment, maximum dose of atoxyl, and total length of atoxyl treatment before symptom was noticed in patients who have become totally blind.

Class of Case on Admission.	Month of Onset.	Length of Treatment.	Amount of Atoxyl.	System Employed	Largest Dose Given.
		Months.	Grammes.		Grammes
B. (m)... ..	September	3	10	(e)	0·7
C. (m)... ..	August ...	1½	4·5	(d)	0·7
B. (m)... ..	November	3	10·5	(e)	0·7
B. (m)... ..	November	2	5	(c)	0·7
C. (m)... ..	October...	6	10·5	(a)	0·4
B. (m)... ..	October...	9	13·5	(a) and (d)	0·7
B. (m)... ..	September	3	8	(d)	0·7
B. (f)	October...	4	8	(c)	0·7
C. (f)	November	3	7·5	(c)	0·7
C. (f)	November	8	8	(a)	0·4
B. (f)	June ...	5	4	(a)	0·4
B. (f)	November	3	10	(c)	0·7
C. (f)	November	1½	5·25	(e)	0·6
C. (f)	November	1½	5·25	(c)	0·6

25. A PRELIMINARY SUMMARY OF THE RESULTS OF THE EXPERIMENTAL TREATMENT OF TRYPANOSOMIASIS IN RATS.

By H. G. PLIMMER, F.L.S., and J. D. THOMSON, M.B., C.M.

[*Reprinted from the PROCEEDINGS OF THE ROYAL SOCIETY, B. Vol. 79.*]

The experiments of which the following is an abstract have been undertaken under the direction of the Tropical Diseases Committee of the Royal Society.

The strains of trypanosomes which have been used in these experiments are a Nagana from the original strain brought to England, and a Surra from Professor Lingard in India. The Nagana strain kills rats in an average time of 5·5 days, and the Surra strain in 6·9 days.

CHINOLIN COMPOUNDS.

The knowledge of the action of quinine in malaria suggested the trial of various chinolin compounds. As is well known, quinine itself has no influence in trypanosomiasis. Cyanin was the substance first tried, as this in extremely dilute solutions (1—10,000) is very poisonous to trypanosomes outside the body. A series of Nagana and Surra rats were given doses of from $\frac{1}{2}$ to 1 milligramme (which is a poisonous dose for small rats), but all of these died about the same time as the controls, and in every case the trypanosomes had increased in the usual manner, so that at death the blood was as swarming with trypanosomes as if no treatment had been used. Messrs Bayer and Co., of Elberfeld, kindly placed at our disposal nine chinolin and chinaldin compounds and six "cyanin farbstoffe," but none of these produced any effect on the development of course of the diseases.

DICHLOROBENZIDINE + ACID H.

This substance, which was first used by Nicolle in trypanosomiasis of mice, was found, when used both on mice and rats, to lengthen the course of the diseases, but in no case was the extension of the course of the disease very marked. Nagana mice, after one dose of 1 c.c. of a 1-per-cent. solution, lived from 8 to 11 days, and Surra mice from 10 to 16 days, one living as long as 29 days; in Nagana rats the disease was prolonged to an average time of 14 days, and in Surra to an average of 16 days. In all the animals treated with this substance the spleen and liver were very much enlarged, and living trypanosomes were found *post-mortem*, showing that the substance had not practically influenced the pathological processes. In no case was the substance completely absorbed.

TRYPANROTH.

This was discovered and first used by Ehrlich. When used alone it lengthened the course of the disease in both Nagana and Surra to about 14 days, but in all cases the spleen was found to be as much enlarged as in the control, and living trypanosomes were invariably found *post-mortem*.

ARSENIOUS ACID.

This was used at first simply dissolved in water, and later, in order to try to avoid the irritation and sloughing invariably produced, in a solution slightly over-neutralised with carbonate of soda. When injected before the fourth day of Nagana and Surra, arsenious acid caused the disappearance of the trypanosomes from the blood, but they invariably recurred before death. It was given in doses of 1 milligramme, and one rat lived as long as 26 days, two to 16 days, and one to 17 days, each of these rats having taken 6 milligrammes altogether. A very considerable effect was produced on the vitality of the trypanosomes, as a rat inoculated from the bone-marrow of one of the 16-day rats did not show trypanosomes in the blood until the ninth day after inoculation. Whether neutralised or not, sores were produced at the points of injection. The spleen was found *post-mortem* to be about as large as that of the controls.

ATOXYL.

This substance, which was first used by Thomas and Breinl, has been found by Ehrlich and Berthelm to be the sodium salt of para-amido-phenyl-arsenic acid, with the formula



and Moore, Nierenstein, and Todd* have confirmed this view of its composition, which differs from that originally published, which stated it to be an anilide of metarsenious acid.

This is the most important substance, so far discovered, in relation to the treatment of trypanosomiasis. In all cases of Nagana and Surra (with the exception of the atoxyl-proof cases mentioned below), atoxyl causes the entire disappearance of the trypanosomes from the blood, so that rats inoculated with the blood when it was microscopically free from parasites failed to take the disease; but the trypanosomes, in our experience, have invariably recurred, and death was only delayed for a period varying with the dose and with the time of commencement of the treatment. When the dose was sufficient, *e.g.*, 1 to 1.5 c.c. of a 5-per-cent. solution in three to five doses (a dose being given every, or every other, day), even after as many as four recurrences the spleen was generally found *post-mortem* to be very little or at most moderately enlarged. A too large dose apparently produced

* "On the Treatment of Trypanosomiasis by Atoxyl . . . followed by a Mercuric Salt," &c., "Biochemical Journal," vol. 2, Nos. 5 and 6.

wasting, and a bad condition of the hair, and, we think, a quicker return of the trypanosomes.

When atoxyl is given more continuously or too freely than is required, in cases in which there have been many recurrences, and probably under some other conditions of which we are ignorant, in a certain small proportion of rats so treated a race of trypanosomes is produced which entirely resists atoxyl, and continues to develop and multiply in spite of continued exhibition of the drug. This strain, when inoculated into fresh rats, retains its resistance to atoxyl. Ehrlich, who has produced such a strain in mice, calls them "atoxyl-fest," and we have obtained this atoxyl-proof variety of trypanosome in rats, both in Nagana and Surra, of which mention will be made later.

1. MONOPHENYLARSENIC ACID.

2. NITROPHENYLARSENIC ACID.

3. PARATOLYLARSENIC ACID.

These three bodies were sent for experimental purposes to Professor Cushny, F.R.S., by Professor Michaelis, who discovered them. They are of interest in connection with the treatment of trypanosomiasis, since atoxyl is an amido derivative of phenylarsenic acid, which was also discovered by Michaelis. They are extremely poisonous substances, and were given in doses of 1 c.c. of a solution of 1/400.

1. Monophenylarsenic acid.—This, in common with other arsenic compounds, notably affected the development of the trypanosomes. In doses of 1 c.c. of 1/400, repeated once or twice in untreated animals, it diminished greatly the number of trypanosomes; and in three recurrent cases, after initial treatment with atoxyl, it caused the trypanosomes to disappear, but it did not save any animal; and it is, as are all these three compounds, poisonous in effective doses.

2. Nitrophenylarsenic acid.—In untreated animals, and in two recurrent cases after atoxyl, this caused a temporary disappearance of the trypanosomes; in a case of second recurrence after atoxyl, it produced no effect on the trypanosomes. It is the most poisonous of the three.

3. Paratolylarsenic acid.—This caused a more effective disappearance of the trypanosomes than the other two compounds, and it was better borne. One Nagana rat, treated only with it from the beginning, lived for 25 days, having had, however, three recurrences during this period. At each recurrence the trypanosomes disappeared after two doses of 1 c.c. of 1/400. In recurrent cases after atoxyl a temporary disappearance of the trypanosomes was also effected.

OTHER ARSENIC COMPOUNDS.

Arrhenal (di-methyl sodium arseniate) and sodium cacodylate were also tried, but were found to have no effect whatever on the course of the disease, nor upon the development of the trypanosomes either in first infections or in recurrences.

OTHER BODIES.

Fluorescein was tried without any effect; and also sodium cinnamate, on account of its reputed property of producing leucocytosis, which might have been useful from the phagocytic standpoint. But it failed to have any effect in these diseases.

TREATMENT WITH TWO OR MORE DRUGS.

The deduction from the above-mentioned experiments with single bodies is that, at the present time, there is no substance known which alone will cause a permanent disappearance of the trypanosomes from the affected animal, *i.e.*, effect a cure; so that experiments have been carried out to see whether any combination of bodies would produce the desired effect. The compounds of mercury seemed from their known properties to be the most promising, and the results of experiments in this direction, lately published by Drs. Moore, Nierenstein, and Todd, are most encouraging. We have not used the form of mercury (liq. hydrarg. perchlor.) with which these good results have been obtained, but we have used the lactate, sozoiolol, and succinimide, and also Donovan's Solution (liq. arsen. et hydrarg. iodid.). Of these the succinimide appears to us to be the best, as it is unirritating, and will apparently mix with atoxyl without change—at any rate it does not interfere with the action of the atoxyl; the lactate is very irritating, even in doses of one-third of a minim of the ordinary hypodermic solution, and it is not so effective as the succinimide; the sozoiolol appears to come between these two in point of efficiency. But in our experience there is a great difference in the individual equation of rats with regard to dosage and poisonous effects, which the consideration of relative weight does not help us to gauge, so that there has been difficulty in ensuring the best method of giving these drugs, and of determining their appropriate quantity. The duration of the disease has been very greatly prolonged in most cases, and in some we have confidence that a cure has been effected.

Of all the substances tried, atoxyl has had by far the most favourable action, and it is easily tolerated, and produces no irritation. But, as mentioned before, it has no permanent effect; it causes the disappearance of the trypanosomes from the blood, even when in very large numbers, but there remain behind certain forms of the parasites which can resist it, and which after an interval can reproduce the general infection with the indifferent forms. These recurrences can take place, in our experience, up to as many as seven times. The resistant forms appear to be located in the intermediate periods in the bone-marrow, but there is some doubt about this yet, as in some cases we have failed to produce an infection, even with a quantity of the marrow. It is probable

also that some of these resistant forms may be found in the glands, and observations are being carried out on these points. But when an infection is produced from the marrow of these atoxyl-treated rats, the incubation period is very much prolonged, and it may be as long as nine days before trypanosomes can be found in the blood of the inoculated animals.

Atoxyl appears to act not by virtue of the arsenic in it alone, but its effects are probably due to this in combination with some other of its constituents, as its action is much more rapid and complete than that of any other of the simpler arsenic compounds which we have tried.

The following Tables I. and II. give the results of treatment with atoxyl and succinimide of mercury: this latter has been given either with the atoxyl or immediately after it, the best method being, we think, to give two or three doses of atoxyl and to give a dose of succinimide of mercury at the same time as the second and third doses, with perhaps one after. Some of our rats have had too much, and we are now giving less with better effect. The succinimide has the great advantage of being unirritating to the tissues, and it will mix with atoxyl without precipitation, and without, at any rate, interfering with the action of the latter.

Table I.—Nagana Rats treated with Atoxyl and succinimide of Mercury. Average duration of untreated disease, 5.5 days.

No.	Weight.	Quantity of 5 p.c. Atoxyl.	Quantity of Succinimide of Mercury.	Recur- rences.	Lived	
	Grammes.	c.c.	Milli- grammes.		Days.	
1	175	2.4	1.5	2	23	Had young on 20th day.
2	210	2.85	1.75	1	30	Did not die of disease.
3	250	2.1	2.5	1	28	Kidneys degenerated.
4	200	2.1	2.75	0	—	<i>Living 143 days.</i>
5	175	2.0	0.75	1	27	Did not die of disease.
6	150	1.8	1.25	0	—	<i>Living 140 days.</i>
7	200	1.8	1.25	0	—	<i>Living 136 days.</i>
8	150	2.75	2.0	6	79	
9	175	2.6	1.25	0	22	Succinimide given too long after the atoxyl.
10	175	3.0	1.25	1	—	<i>Living 92 days.</i>
11	125	1.8	0.8	0	38	
12	200	1.2	0.75	1	—	<i>Living 85 days.</i>
13	160	2.8	0.75	3	36	
14	210	4.5	1.75	4	59	
15	175	1.75	0.5	0	—	<i>Living 78 days.</i>
16	190	1.4	0.25	0	—	<i>Living 75 days.</i>
17	200	4.1	1.75	4	42	Trypanosomes plentiful at time of death, probably atoxyl-proof.
18	175	6.35	2.0	7	107	This rat had 5 minims. of Donovan's solution on the initial appearance of trypanosomes, but, as it had no effect, atoxyl, and subsequently succinimide, were given.
19	160	4.1	0.75	3	61	
20	150	3.7	0.5	3	44	Given paratolylarsenic acid after third recurrence, which killed the rat.
21	150	0.7	0.75	0	—	<i>Living 37 days.</i>

Table II.—Surra Rats treated with Atoxyl and Succinimide of Mercury. Average duration of untreated disease, 6·9 days.

No.	Weight.	Quantity of 5 p.c. Atoxyl.	Quantity of Succinimide of Mercury.	Recur- rences.	Lived.	
	Grammes	c.c.	Milli-grammes.		Days.	
1	175	1·5	2·25	0	43	Did not die of disease.
2	175	1·5	2·25	0	68	Did not die of disease.
3	150	1·5	1·25	0	44	Did not die of disease.
4	200	5·1	2·75	3	63	
5	125	1·8	1·5	0	—	<i>Living 137 days.</i>
6	125	1·8	0·5	0	120	Did not die of disease.
7	155	1·8	0·75	1	24	
8	175	2·45	1·0	1	23	This quantity of succinimide produced an acute nephritis in this rat, with necrosis of the epithelium of the convoluted tubes, and many hæmorrhages.
9	160	3·3	1·0	1	—	<i>Living 91 days.</i>
10	150	3·0	0·75	4	55	
11	150	2·4	0·75	2	32	
12	160	2·1	0·37	1	22	Treatment suspended on 10th day.
13	160	1·8	0·25	2	32	Did not die of disease.
14	145	2·1	0·75	0	—	<i>Living 42 days.</i>
15	120	1·9	0·5	0	—	<i>Living 39 days.</i>
16	125	3·0	1·0	2	34	This rat had 2 c.c. iodipin on 3rd day.
17	200	4·1	1·75	4	42	
18	145	1·05	0·25	0	—	<i>Living 42 days.</i>
19	120	0·95	0·5	0	—	<i>Living 39 days.</i>
20	145	1·05	0·65	0	—	<i>Living 33 days.</i>
21	125	2·1	0·75	3	54	This rat had at the outset 8 mgms. in all of arsenious acid, the atoxyl being given on the first and subsequent recurrences.
22	155	1·5	1·0	1	32	This rat had also initial treatment with arsenious acid, of which it had 6 mgms. in all, the atoxyl being given on the first recurrence. The rat did not die of the disease, but from injury during pregnancy.

(See also No. 8, Table III.)

Table III. gives the results of treatment with atoxyl and mercury soziodol, from which it will be seen that the results are not so good as those with succinimide of mercury. Mercury soziodol will not mix with atoxyl, a dense precipitate being formed when the solutions are mixed. The solution used was the ordinary hypodermic solution (1·5 per cent.) prepared by Martindale.

Table III.—Nagana and Surra Rats treated with Atoxyl and Mercury Soziodol. Average duration of untreated diseases 5·5 and 6·9 days respectively.

Disease.	No.	Weight.	Quantity of 5 p. c. Atoxyl.	Quantity of Mercury Soziodol.	Recur- rences.	Lived.	
		Grammes.	c.c.	Minims.		Days.	
Nagana	1	200	1·35	1	1	24	<i>Living 108 days.</i>
	2	150	1·4	1	1	26	
	3	145	1·8	1	0	—	
	4	155	2·4	1 $\frac{1}{3}$	1	26	
	5	275	1·8	1 $\frac{1}{3}$	0	—	<i>Living 122 days.</i> <i>Did not die of disease.</i>
	6	150	1·8	1	0	35	
	7	315	5·7	1 $\frac{2}{3}$	4	59	
	8	150	6·8	1 $\frac{2}{3}$	7	81	
Surra ..	9	150	2·7	$\frac{2}{3}$	1	33	After second recurrence with mercury soziodol, succinimide of mercury was substituted, of which 0·75 mgm. was given in all. After first recurrence, this rat was given succinimide of mercury, of which it had 1 mgm. in all.

Table IV. gives the results of treatment with atoxyl and lactate of mercury, which are less good than those with succinimide and soziodolate of mercury. This drug has the disadvantage of being very irritating to the tissues, and also of forming a precipitate when mixed with atoxyl. The solution used was the ordinary hypodermic solution (2·5 per cent.) prepared by Martindale.

Table IV.—Nagana and Surra Rats treated with Atoxyl and Lactate of Mercury. Average duration of untreated diseases, 5·5 and 6·9 days respectively.

Disease.	No.	Weight.	Quantity of 5 p. c. Atoxyl.	Quantity of Lactate of Mercury.	Recur- rences.	Lived.	
		Grammes.	c.c.	Minims.		Days.	
Nagana	1	175	1·85	1	1	25	<i>This rat had 0·5 mgm. of succinimide of mercury after first recurrence.</i>
	2	150	2·1	1	1	26	
	3	150	1·5	1	0	23	
	4	175	3·65	1	1	31	
Surra ..	5	200	3·9	1	1	32	<i>Did not die of disease.</i> <i>This rat had 1 mgm. of succinimide of mercury after first recurrence.</i>
	6	275	3·45	1	1	30	
	7	175	1·2	1	0	21	
	8	315	3·6	1	1	24	
	9	125	3·0	$\frac{2}{3}$	2	35	

Table V. gives the results of a few experiments made with atoxyl and Donovan's solution (lig. arsenic et hydrarg. iodid.) which are somewhat encouraging. During the last month a fresh and more extensive series of experiments have been started. The poisonous effects of Donovan's solution show themselves in the intestines, which become intensely inflamed, whereas the effects of too large doses of succinimide of mercury show themselves principally in the kidney, in the form of an

acute inflammation going on to necroses with multiple hæmorrhages.

Table V.—Nagana and Surra Rats treated with Atoxyl and Donovan's Solution. Average duration of untreated diseases, 5·5 and 6·9 days respectively.

Disease.	No.	Weight.	Quantity of 5 p. c. Atoxyl	Quantity of Donovan's Solution.	Recur- rences.	Lived.	
Nagana	1	Grammes. 130	c.c. 1·8	Minims. 5	2	Days. 38	This rat had 25 c.c. 1·400 monophenylarsenic acid after first recurrence; this removed the trypanosomes from the blood, but a second recurrence took place 11 days later.
	2	175	3·7	17	4	—	Living 67 days.
	3	150	2·4	15	3	72	
	4	200	2·25	4 + 0·5 c.c.	1	28	
Surra ..	5	190	2·25	5	1	23	The 0·5 c.c. of Donovan's solution was given to test dosage.* Next day the rat became very ill, and died two days after with acute enteritis. No kidney lesion.
	6	300	1·0	8	0	—	
							Living 36 days.

* See paper by Drs. Moore, Nierenstein, and Todd, before referred to.

Table VI. gives the results of a series of experiments made with atoxyl and iodipin. This latter is a solution, or mixture, of iodine in oil of sesame, made by Merck, who kindly placed some at our disposal, and it is stated to be unirritating, and it can be given in large doses with safety. The results are sufficiently encouraging to suggest a further trial of this combination. The oil takes a very long time to get absorbed; it becomes colourless from absorption of the iodine, and appears to cause no irritation in the tissues.

Table VI.—Nagana and Surra Rats treated with Atoxyl and Iodipin. Average duration of untreated disease, 5·5 and 6·9 days respectively.

Disease.	No.	Weight.	Quantity of 5 p. c. Atoxyl.	Quantity of Iodipin.	Recur- rences.	Lived.	
		Grammes.	c.c.	c.c.		Days.	
Nagana	1	275	4·9	7·5	2	35	Did not die of disease.
	2	150	5·4	9·5	5	71	
	3	150	1·8	6·0	0	26	
	4	195	1·5	2·0	0	112	
	5	175	2·1	6·0	2	23	
	6	275	4·0	7·5	0	29	
	7	175	4·5	7·0	3	44	
	8	175	1·9	4·0	0	57	
	9	195	1·5	2·0	0	—	Had eight young towards end of treatment.
	10	195	1·5	2·0	0	—	Living 132 days.
	11	143	6·6	12·0	2	44	Living 132 days.
Surra ..	12	250	4·1	1·0	1	29	Did not die of disease.
	13	250	4·0	4·0	2	21	
	14	215	4·5	6·5	0	—	Living 103 days.
	15	165	2·9	4·5	2	33	
	16	150	3·3	6·0	2	31	Did not die of disease.
	17	150	1·8	2·5	1	20	Did not die of disease.

THE PRODUCTION OF AN ATOXYL-PROOF RACE OF TRYPANOSOMES IN RATS.

This phenomenon is of great biological and therapeutical interest, and needs much further research yet, both for its explanation, and its bearing on treatment.

In certain rats, after treatment with atoxyl, a number of recurrences may take place—we have seen as many as seven; these recurrences at first yield to treatment with atoxyl, but as the case progresses towards its end, the recurrences occur at shorter and shorter intervals, until one comes to a time when they can be no longer affected by atoxyl. The trypanosomes in this case have become atoxyl-proof. Ehrlich succeeded in producing an atoxyl-proof strain of Nagana in mice, and we have succeeded in producing atoxyl-proof strains of both Nagana and Surra in rats. One point of importance biologically is that these atoxyl-proof trypanosomes do not lose their resistance to atoxyl on transference into other rats, and we have carried this strain on in Nagana through a series of eight successive rats, and in Surra through a series of six rats without any loss of their atoxyl-proof properties. When treated with atoxyl, even in large doses, multiplication goes on just as rapidly as in untreated animals, and the rats die at the usual time. Our cases have been given atoxyl to test them, and have been then treated with various substances, as set forth in the table below. Of these substances, trypanroth and some form of mercury have given the best results. In thinking of human trypanosomiasis in this connection, the danger of the production of an atoxyl-proof strain will be at once apparent: so that atoxyl should be given to human beings with the greatest care and forethought.

The following Table VII. summarises the few results we have obtained so far. Rat No. 1 was inoculated from a Nagana rat which had become uninfluenced by atoxyl after the third recurrence, before which large and repeated doses had been given: and Rat No. 11 was inoculated from a Surra rat in a similar condition.

Table VII.—Summary of Results obtained with Atoxyl-proof Strains of Nagana and Surra in Rats.

Disease.	No.	Weight.	Trypanroth 1 per cent.	Succinimide of Mercury.	Donovan's Solution.	Dichloro- benzidine + Acid H 1 per cent.	Paratolyl- arsenic Acid 1/400.	Lived.	
Nagana	1	Grammes. 130	c.c. —	Milligrammes. —	Minims. —	c.c. —	c.c. —	days. 6	Treated only with atoxyl.
	2	150	—	—	—	—	—	6	Treated only with atoxyl.
	3	140	—	0.25	—	—	—	6	Did not influence the course of the disease.
	4	250	5	0.5	—	—	2	17	Trypanroth caused a disappearance of the trypanosomes for 6 days: paratolylarsenic acid did not affect them.
	5	200	6	0.5	—	—	2	11	Neither trypanroth nor paratolyl-arsenic acid did more than restrain for a few days the multiplication of the trypanosomes in this case.
	6	175	—	0.75	—	6	1	10	Dichloro benzidine + acid H caused the trypanosomes to disappear for 3 days.
	7	150	—	—	—	—	2	6	Trypanosomes were not affected.
	8	125	4	—	8	—	—	14	Trypanosomes driven out of the blood for 5 days.
	9	175	6	—	6	—	—	12	Trypanosomes driven out of the blood for 3 days.
	10	225	3	—	4	—	—	10	Trypanosomes only disappeared the day before death.
	11	125	—	—	—	—	—	3	Did not die of disease.
Surra ...	12	150	3	—	—	—	—	5	
	13	125	3	—	—	—	—	6	
	14	105	3	0.62	—	—	—	10	

[Reprinted from the PROCEEDINGS OF THE ROYAL SOCIETY,
B. Vol. 80.]

26. FURTHER RESULTS OF THE EXPERIMENTAL
TREATMENT OF TRYPANOSOMIASIS IN
RATS; BEING A PROGRESS REPORT OF A
COMMITTEE OF THE ROYAL SOCIETY.*

By H. G. PLIMMER, F.L.S., and J. D. THOMSON, M.B., C.M.

(Communicated by Sir Ray Lankester, K.C.B., F.R.S., Chair-
man of the Tropical Diseases Committee. Received
October 28th,—Read November 7th, 1907.)

[PLATE 1.]

The following results are a continuation of the work already
described, and the experiments have been carried out upon rats
inoculated with the same strains of Nagana and Surra:—

CONDITION OF THE ANIMALS LIVING AT THE DATE OF THE
COMPLETION OF THE TABLES IN THE FORMER PAPER.

Table I.—Nagana rats treated with Atoxyl and Succinimide
of Mercury.

No. 4 is still living and well 229 days after inoculation.

„ 7	„	„	222	„	„
„ 10	„	„	178	„	„
„ 15	„	„	164	„	„
„ 21	„	„	63	„	„
„ 6 died on the 214th day after inoculation.					
„ 12	„	110th	„		
„ 16	„	81st	„		

In these rats the livers were found to be pale and fatty, and
the kidneys degenerated: these were pale and fatty, with
fibrous streaks, and the urine of Nos. 12 and 16, found in the
bladder *post-mortem*, contained albumen. They did not die of
the disease, as no trace of trypanosomes could be found in
either of them, but of the degenerative changes mentioned.

* This Committee, which planned and supervised the investigations, was
appointed by the Tropical Diseases Committee for the purposes of this
experimental enquiry, and consists of the following members:—Professor
J. Rose Bradford, Colonel Bruce, Professor Cushny, and Mr. H. G. Plimmer.
A preliminary summary of the results of the enquiry has already appeared
in the "Proceedings of the Royal Society" (B, vol. 79, 1907, pp. 505–516).
By the courtesy of the governing body of the Lister Institute the investiga-
tions have been carried on in the laboratories of that institution.

Table II.—Surra rats treated with Atoxyl and Succinimide of Mercury.

No. 5	died on the 206th day	after inoculation, of pneumonia.
„ 9	„ 169th	„ „ „
„ 14	„ 61st	„ from an unnoticed recurrence.
„ 15	„ 59th	„ from paralysis after three recurrences.
„ 18	„ 61st	„ .
„ 19	„ 59th	„ .
„ 20	„ 57th	„ after five recurrences, becoming finally atoxyl-proof.

In Nos. 5 and 9 there was also evidence of fatty and fibrous degeneration of the kidneys.

Of these rats only in Nos. 14 and 20 was there any evidence that they died of the disease.

Table III.—Rats treated with Atoxyl and Mercury Sozoiodol.

No. 5 is still living and well, 208 days after inoculation.

„ 3 died on the 181st day after inoculation.

(The kidneys and liver of No. 3 were very fatty.)

Table V.—Rats treated with Atoxyl and Donovan's Solution.

No. 2 died on the 70th day after inoculation.

„ 6 „ 121st „ „

(The kidneys of No. 2 were degenerated, those of No. 6 markedly so, being pale in colour with yellow streaks, and very friable; there was albumen in the urine.)

Table VI.—Rats treated with Atoxyl and Iodipin.

No. 9 is still living and well 218½ days after inoculation.

„ 10 died on the 141st day after inoculation.

„ 14 „ 178th „

(No. 14 had also 1·2 milligrammes of succinimide of mercury. The kidneys of this rat were degenerated, and it had albumen in its urine.)

From the above list it will be seen that the principal pathological lesion in those rats which have been treated with atoxyl and some compound of mercury and have lived for a very long time after inoculation, being, we think, cured of the disease, is a degeneration of the kidneys; and in most of these rats this was the only lesion found *post mortem*. This will be referred to later in mentioning further treatment with mercury.

ATOXYL AND CALOMEL.

Twelve rats have been treated with atoxyl (three to five doses) and then with subcutaneous and intramuscular injections of calomel, in doses of 1 minim of Colonel Lambkin's formula. It is difficult in rats to make the injection into the muscles, and in all cases necrosis occurred at the site of the injection; no better result was attained than by treatment with atoxyl alone, with subsequent recurrences and death.

ATOXYL AND SUCCINIMIDE OF MERCURY.

Further experiments have been made with this combination, in which the dose of the mercury salt has been increased up to 1 milligramme. The 12 rats of this series are all dead, and showed acute kidney changes: inflammation, going on to necrosis of the epithelium, multiple hæmorrhages, etc.

ATOXYL AND DONOVAN'S SOLUTION.

Nine further experiments have been made with this combination, also in larger doses; but these larger doses have been invariably fatal, with lesions both of the intestines and kidneys. The doses were arranged upon the basis of the doses recorded, with such good results, by Drs. Moore, Nierenstein, and Todd;* but one of us has received a letter, since the experiments were completed, from Dr. Nierenstein, stating that the Donovan's solution used in their experiments was diluted with an equal part of water.

ATOXYL AND LIQ. HYDRARG. PERCHLOR.

A series of 12 rats was treated with this combination on the lines laid down in the paper above referred to, by Drs. Moore, Nierenstein, and Todd. The results obtained by them gave much hope that this combination would be especially useful. But we have not been able to get such good results. Out of 12 rats so treated only one is alive at the 97th day, the others having died with acute renal lesions. Of course, really comparative results are always difficult to obtain, and in rats the individual equation, with regard to dosage, and to resistance both to drugs and to disease, is a very varying one. We have, for instance, found, with the rats we have used, that the white ones are more susceptible both to diseases other than trypanosomiasis and to drugs than the black and white ones are; and we find the grey are the least susceptible.

From the above, considering both those experiments recorded in our former paper which have since ended fatally, and the more recent and—as regards dosage—bolder experiments, we are forced to the conclusion that, in small animals at any rate, mercury has not in our hands given altogether satisfactory results. Perhaps it may be a question of dosage; we have, however, tried to enlarge the range of dosage, as far as possible, from homœopathic doses to large ones, without attaining a large percentage of cures. If the dose of mercury be sufficient to aid the atoxyl, as in the cases brought forward from our last paper, we have found, in those cases which have died, chronic kidney, and in a less degree liver, lesions, which seem to be the late result of those more acute changes which

* "On the Treatment of Trypanosomiasis by Atoxyl . . . followed by a Mercurial Salt, &c.," "Biochemical Journal," vol. 2, Nos. 5 and 6.

we have found in those animals which have died earlier, either from disproportionate dosage or from some want of resistance to the drug.

Perhaps, in dealing with a more chronic trypanosome disease such as Sleeping Sickness in man, the results would be more favourable. We have, for instance, two Sleeping Sickness rats, inoculated on April 15, which have been treated with quite small doses of atoxyl and succinimide of mercury, and in which no trypanosomes have been found since May 4; they appear to be quite well. We have also another Sleeping Sickness rat, inoculated on May 6, which has been treated only with atoxyl, and in which no trypanosomes have been found since May 28. But in the more acute forms of trypanosomiasis, such as Nagana and Surra, the method of treatment by atoxyl and some form of mercury has, in our experience, almost invariably led to degenerative lesions, principally in the kidneys, which has been a cause of death long after any trace of trypanosomes could be found, when we have believed that the animal has been quite cured of the initial disease.

TIODINE.

A few rats were treated with this substance, which is thiosinaminethyliodide ($C_6SN_2H_{13}I$). In doses of 10 minims it is immediately fatal to rats, although it is stated to be non-poisonous to man, and in doses of 5 minims caused death within 24 hours; in smaller doses, alone or in combination with atoxyl, it had no influence on the disease.

CERTAIN ANTIMONY COMPOUNDS.

The treatment with arsenic compounds was, as has been stated, attended with only partial success. Professor Cushny, F.R.S., who has advised us on pharmacological matters throughout these investigations, sent us for trial a weak combination of glycine and antimony, attempts to form an antimony compound analogous to atoxyl having failed. When injected into inoculated rats, the antimony glycine was found to possess, in a less degree, the power of the antimony compounds described below; it reduced the number of trypanosomes, and caused their disappearance from the blood for a time, if they were not very numerous.

But the combination was difficult to make, varied in strength, and its solution was very dilute, and its use was abandoned when it was found that the other antimony compounds, described below, were so much more effectual

POTASSIUM ANTIMONYL TARTRATE.

Potassium antimonyl tartrate (tartar emetic), which is easily soluble, was then tried. In doses of 1 c.c. of a 1 per cent. solution it proved fatal within 24 hours to four inoculated rats

of weights varying from 190 to 225 grammes, but it was noticed that the trypanosomes had greatly diminished in number. It was also noticed that the rats appeared to be ill and faint for a short time after the injection: they were unsteady and sometimes rolled about. This was at the time attributed to the depressing effect of the potassium in the compound, and suggested the making and using of the substance described below, with which all of our experiments have so far been done. The question of the effect of this particular salt on the rats themselves will be mentioned later. Experiments are in progress for the purpose of comparing the actions of the potassium and sodium compounds: the latter would seem to possess some theoretical advantage, especially in treating larger animals, when the dose will have to be proportionally larger.

SODIUM ANTIMONYL TARTRATE.

Through the kindness of Dr. R. H. Aders Plimmer, of University College, we have been able to obtain and use this compound, which is the sodium salt corresponding to potassium antimonyl tartrate. He has prepared a quantity of the pure substance for us, in crystalline form, and has written the appended Note* upon its chemistry.

This substance in 1 per cent. solution is that which, of all the various bodies mentioned in these papers, including atoxyl, has the most marked and remarkable influence upon trypanosomes in the living body. Although our experiments with it are not many, nor of long duration, the results so far seemed sufficient to induce us to call the attention of other workers in this field to it.

The injection of this compound causes no pain, nor does it produce any inflammation of the tissues; and the results of the injection are very striking. The trypanosomes disappear with great rapidity from the blood, and in the majority of the cases treated so far there has been no recurrence; and inoculations made from animals which have been killed, or have died, have been invariably negative. It acts much more quickly than atoxyl, and its dose is very much smaller, and it does not produce any undesirable effects on the animals, and recurrences are very much less frequent than is the case when atoxyl has been used.

We have used a 1 per cent. solution of the solid salt, but this is quickly invaded by moulds, and needs the addition of a crystal of thymol, or of 0.25 per cent. of formalin. The question of dosage is still under observation. We have tried many ways, and at present we are inclined to think that a full dose (*e.g.*, 0.5 c.c. of a 1 per cent. solution for a rat of 200 grammes or over) should be given when the trypanosomes are

* See Note at end of paper, p. 117.

fairly plentiful in the blood, and then repeated at intervals of one, two, and three days, up to about four doses, and thereafter in weekly doses for a month. But we have good results in cases in which a dose has been given on four successive days, also when given every other day, and so on up to once every five days, without any recurrence up to as many as 52 days; but of two cases dosed at five-day intervals, one has recurred and one has not. As regards the quantity which can be taken, we have one rat of 130 grammes weight which has taken 0.5 c.c. of a 1 per cent. solution on the 3rd day (when trypanosomes were plentiful in the blood), and again on the 5th, 0.29 c.c. on the 6th and 7th days, and 0.25 c.c. on the 8th, 9th, 10th, 12th, 13th, 14th, 15th, 16th, 17th, and 19th days, and it is still living and well on the 43rd day, and has had no recurrence. When it is given in a full dose for the first time to rats whose blood is swarming with trypanosomes, the rat generally becomes very restless, and rolls about; its respirations become very quick, and it appears to be ill. These symptoms were noticed in the initial experiments with tartar emetic, and were attributed to the potassium contained in it, but we think that they are more probably due to the changes in the blood caused by the destruction or solution of the trypanosomes, which occurs very rapidly, as they do not occur after the second dose, when there are no trypanosomes. Recovery has, so far, always taken place from this condition, but it would seem advisable, in cases where the first dose is delayed until the blood is swarming with trypanosomes, to give the dose in two halves at intervals of a few hours.

The quickness of the action of sodium antimonyl tartrate is very remarkable. In one rat, whose blood was swarming with trypanosomes, a dose of 0.35 c.c. of a 1 per cent. solution caused their entire disappearance from the blood within half an hour; and in two other cases, in which the blood contained very large numbers of trypanosomes, after injection of 0.33 c.c. only a few could be found at the end of half an hour, and in one after an hour none could be found, and in the other only one in an ordinary blood preparation (see Plate 1). In these cases a few trypanosomes can sometimes be found in the liver, and these are extremely active and in no way inconvenienced by the drug; whether these are the forms which can persist, and need to be tired out by successive doses, we cannot say at present, but their extreme activity, when all the others has disappeared, is suggestive. We have up to the present not detected any morphological differences in them.

A striking instance of the power of this compound over trypanosomes is seen in the case of a guinea-pig which was inoculated with *Trypanosoma gambiense* on April 9. From July 3 to September 16, trypanosomes were present in the blood, latterly in quantity, and the animal was dying on September 16; its eyelids were œdematous and nearly closed: it had œdema of the genitals and anus, and a discharge of

bloody mucus from the rectum, and its hair was coming out in large patches. At this date—September 16—is was given 0.5 c.c. of a 1 per cent. solution; on the 17th the trypanosomes had entirely disappeared, and 0.75 c.c. was given; on the 19th the animal to all appearances was quite well, and on this day, and on 21st and 26th, 1 c.c. was given. The œdema disappeared and it continued to look well, and showed no more trypanosomes. It lived until October 14, when it died; *post-mortem* the organs were congested and the kidneys were inflamed and the urine in the bladder contained albumen. The fact that the guinea-pig was moribund when the treatment was commenced may reasonably account for the pathological condition.

The following table shows the general results, as obtained so far, of the treatment with sodium antimonyl tartrate. Of the 39 rats enumerated in this table, the first 3 had been treated at first with antimony glycine; and of the 11 of the remaining 36 which have died, 6 did not die of the disease, and there remain alive and well 3 of 52 days, 1 of 49, 7 of 44, 8 of 43, 4 of 31, and 2 of 21; and of these 25, 23 have had no recurrence. It will be seen that 8 of the rats (4 Nagana and 4 Surra) have been treated with mercury in addition to the sodium antimonyl tartrate, in order to see if these obtained thereby any advantage over those not so treated. So far as we can tell at present, there seems to be no obvious advantage: one of the Nagana rats treated with liq. hydrarg. perchlor. has had three recurrences, and one Surra rat treated with succinimide of mercury has died after one recurrence.

SODIUM ARSENYL TARTRATE.

As the results with the sodium antimonyl tartrate were so definite, it seemed worth while to investigate the effect of the corresponding arsenic compound.

Table of Nagana and Surra Rats treated with Sodium Antimonyl Tartrate. Average duration of untreated diseases 5.5 and 6.9 days respectively.

Disease.	No.	Weight in Grammes.	Total amount of 1 per cent. Sodium Antimonyl. Tartrate in c.c.	Result to Oct. 24.	Recurrences.	Remarks.
Nagana	1	150	6.2	Died on 49th day	2	Antimony glycine had been given at first, sodium antimonyl tartrate on first recurrence.
"	2	200	0.83	" 25th "	1	" "
"	3	170	1.75	" 35th "	1	No trypanosomes were found for 12 days before or at death. Antimony glycine had been given at first, sodium antimonyl tartrate on first recurrence. No trypanosomes found for 10 days before, or at death, and a mouse inoculated with bone marrow did not take the disease.
"	4	115	2.76	" 38th "	1	No trypanosomes found for 16 days before, or at death. Rat became paralysed.
"	5	175	1.35	" 16th "	1	Probably too small a dose.
"	6	125	1.0	" 18th "	2	" "
"	7	200	3.0	Living 52 days ...	0	" "
"	8	150	2.5	" 52 "	0	" "
"	9	250	2.6	" 52 "	0	" "
"	10	215	3.5	" 49 "	0	" "
"	11	125	2.6	Died on 22nd day	1	Died of septicæmia from sloughing tail, not of disease. No trypanosomes found.
"	12	195	3.25	" 19th "	0	" "
"	13	175	1.85	" 40th "	0	Died of septicæmia from an abdominal abscess, not of disease. No trypanosomes found.
"	14	110	1.9	Living 43 days ...	0	" "
"	15	130	3.6	" 43 "	0	This rat had 14 doses in 19 days, <i>vide p.</i>

31544	"	16	155	1.5	"	43	"	...	0	No trypanosomes found <i>post mortem</i> .
	"	17	120	1.15	"	43	"	...	0	
	"	18	225	3.75	Died on 31st day				2	
	"	19	140	1.48	<i>Living</i> 43 days ...				0	
	"	20	125	3.75	"	43	"	...	3	
	"	21	150	1.5	"	43	"	...	0	
	"	22	125	1.5	Died on 27th day				1	
	"	23	125	1.1	<i>Living</i> 43 days ...				0	
	"	24	150	2.5	Died on 28th day				1	
	"	25	115	1.8	<i>Living</i> 31 days ...				0	
	"	26	125	2.1	"	31	"	...	0	
	"	27	125	2.1	"	31	"	...	0	
	"	28	140	2.0	"	31	"	...	0	
	"	29	190	1.5	"	31	"	...	0	
	"	30	150	1.4	"	21	"	...	0	
	"	31	275	.0	"	21	"	...	0	
	Surra	32	175	1.9	<i>Living</i> 44 days ...				1	
	"	33	175	1.5	"	44	"	...	0	
	"				"	44	"	...	0	
	"	34	175	1.5	"	44	"	...	0	
	"	35	200	2.0	"	44	"	...	0	
	"				"	44	"	...	0	
	"	36	150	1.5	"	44	"	...	0	
	"	37	175	3.4	Died on 37th day				0	
					<i>Living</i> 44 days ...				0	
	"	38	250	4.0	Died on 11th day				0	
	"	39	250	2.0					0	

Sodium Arsenyl Tartrate or Sodium Tartrarsenite.—This compound was investigated by Henderson and Ewing* in 1895, who gave it the formula $\text{AsONaC}_4\text{H}_4\text{O}_6 \cdot 2\frac{1}{2}\text{H}_2\text{O}$.

It was prepared for these experiments by dissolving one equivalent of arsenious oxide in two equivalents of acid sodium tartrate, filtering, evaporating to a small volume, and adding alcohol till crystallisation commenced; on cooling, the substance crystallised out.

This substance does not seem to be anything like so effective as the antimony compound. Of five rats which have been treated with it, four died between the 12th and 24th days, and three of these had a recurrence; one is still living on the 21st day, but we think that this is probably due to the sodium antimonyl tartrate which was given after a recurrence, in the same way as if from the beginning of the disease.

A mixture of equal parts of a 1 per cent. solution of sodium antimonyl tartrate and of sodium arsenyl tartrate has been tried on six rats. One died on the 14th day and the five others are still living on the 21st day without any recurrence.

IMMUNITY.

With a view of ascertaining what amount of immunity, if any, had been conferred on an animal which we considered to be cured, a Nagana rat was taken which was inoculated on May 13, and had been afterwards successfully treated with atoxyl and succinimide of mercury, and in which no trypanosomes had been found since it had its first dose on May 16, when the trypanosomes were very plentiful in the blood. On October 7, the 147th day, the rat was re-inoculated from another Nagana rat, and on the 11th trypanosomes were present in numbers in the blood; a dose of sodium antimonyl tartrate was given and no trypanosomes have been seen since the 12th. This seems to point to the fact that no immunity is conferred.

DESCRIPTION OF PLATE.

The microphotographs were made from rough blood-preparations, with a low-power objective (Zeiss 8 mm.), in order to demonstrate the rapid disappearance of the trypanosomes from the blood after administration of sodium antimonyl tartrate.

FIG. 1 shows the blood of a Nagana rat, 4 days after inoculation *before treatment*.

FIG. 2 shows the blood from the same rat *half an hour* after the injection of 0.35 c.c. of a 1 per cent. solution of sodium antimonyl tartrate.

FIG. 3 shows the blood from the same rat *one hour* after administration of the above dose.

* Henderson and Ewing "Chem. Soc. Trans.," 1895, vol. 67, p. 103.

FIG. 1.



FIG. 2.

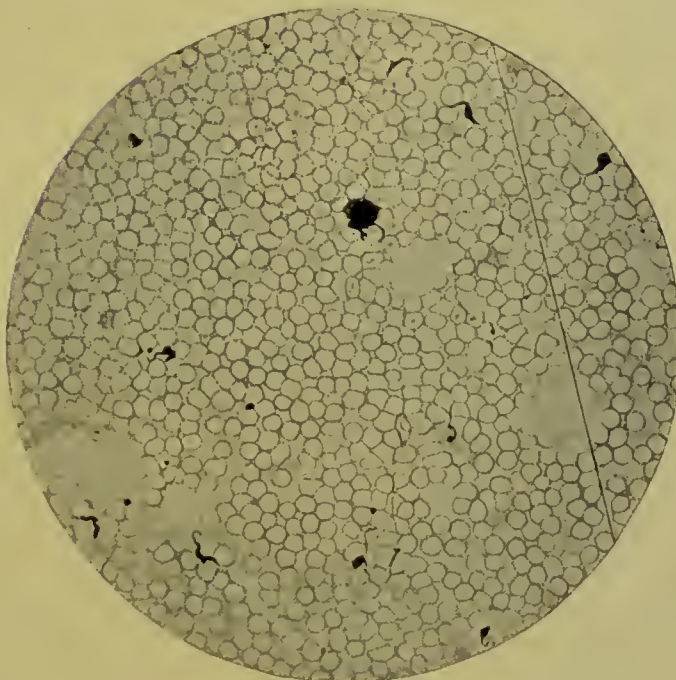
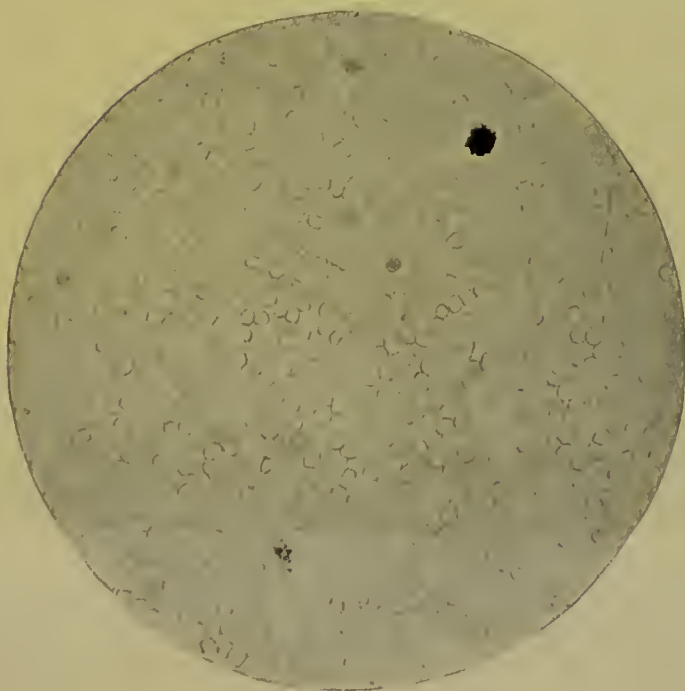


FIG. 3.



27. NOTE UPON SODIUM ANTIMONYL TARTRATE.

By R. H. ADERS PLIMMER, D.Sc. LOND.

Sodium antimonyl tartrate was described in 1842 by Dumas and Piria,* who gave it the constitution $C_8H_8O_{10}NaO$, $Sb_2O_3H_2O$,† but did not state how they had prepared it. Clarke and Evans‡ obtained a compound of the composition $3Na_2C_4H_4O_6 + 2Sb(OH)_3 + 3H_2O$, in 1883, by saturating tartaric acid with antimony trioxide and neutralising the solution with sodium carbonate. The first compound does not seem to have been prepared again since 1842.

Sodium antimonyl tartrate was prepared according to the methods usually given for preparing tartar emetic, by boiling a solution of acid sodium tartrate (13 grammes) with a little more than the calculated quantity (10 grammes) of antimony trioxide until the latter had almost completely passed into solution. On filtering and concentrating the solution to a small volume no crystallisation occurred, but on adding a little alcohol the whole became solid. This was then dissolved in about twice its volume of hot water, and alcohol was added until precipitation commenced, when, on cooling, the sodium antimonyl tartrate crystallised out. This compound at the ordinary temperature dries very slowly and has a moist appearance, but when dried *in vacuo* over sulphuric acid it becomes anhydrous and loses $2\frac{1}{2}$ molecules of water of crystallisation, resembling sodium tartrarsenite in this respect. The substance is very easily soluble in water and its solution reacts faintly acid to litmus.

0.7228 gramme air-dried substance lost *in vacuo* over sulphuric acid 0.0920 gramme $H_2O = 12.73$ per cent.

1.0538 gramme air-dried substance lost *in vacuo* over sulphuric acid 0.1338 gramme $H_2O = 12.70$ per cent.

Calculated for $C_4H_4O_7NaSb.2\frac{1}{2}H_2O$. $H_2O = 12.8$ per cent.

I. 0.4058 gramme substance dried *in vacuo* over sulphuric acid gave 0.2332 gramme Sb_2S_3 and 0.0974 gramme Na_2SO_4 .

II. 0.3780 gramme substance dried *in vacuo* over sulphuric acid gave 0.2072 gramme Sb_2S_3 and 0.0912 gramme Na_2SO_4 .

Calculated for $C_4H_4O_7NaSb$. $Sb = 39.09$ per cent.; $Na = 7.49$ per cent.

Found:—I. $Sb = 39.28$ per cent.; $Na = 7.77$ per cent.

II. $Sb = 39.14$ „ $Na = 7.81$ „

* Dumas and Piria "Liebig's Annalen," 1842, vol. 44, p. 89.

† Old notation.

‡ Clarke and Evans "Berichte," 1883, vol. 16, p. 2385.

When dried at 105° C., the substance loses only two molecules of water of crystallisation :—

0.6120 gramme air-dried substance lost at 105° C. 0.0640 gramme H_2O = 10.46 per cent.

Calculated for $\text{C}_4\text{H}_4\text{O}_7\text{NaSb} \cdot 2\text{H}_2\text{O}$. H_2O = 10.49 per cent.

The remaining half molecule is subsequently lost *in vacuo* over sulphuric acid.

0.6120 gramme substance dried at 105° C. then lost *in vacuo* over sulphuric acid 0.0110 gramme H_2O . Total loss = 12.25 per cent.

On exposure to air, the two and a half molecules of water of crystallisation are again taken up, but the salt does not deliquesce.

0.5370 gramme substance dried *in vacuo* over sulphuric acid, on exposure to air increased in weight to 0.6066 gramme.

28.—INDEX

TO THE FIRST NINE REPORTS OF THE SLEEP-
ING SICKNESS COMMISSION OF THE ROYAL
SOCIETY.

BY LADY BRUCE, R.R.C.

Subject.	Report.	Page.
Abyssinian or East African Animal Disease (<i>see under</i> Animal Experiments)...	No. 5.	22
" " " " " " " "	No. 6.	111
Administrative measures, intended to prevent the spread of disease, and medical measures to cure those already afflicted	No. 9.	62
Age, influence of, in sleeping sickness	No. 2.	18
" " " " " " " "	No. 3.	26
Albert Lake—Fly-belt infected with sleeping sickness ...	No. 6.	6
" <i>Glossina palpalis</i> , distribution round	No. 6.	273
" Presence of <i>G. palpalis</i>	No. 8.	87
" Presence of sleeping sickness	No. 8.	86
Alimentary system	No. 2.	27
" " See cases	No. 1.	39
" " " " " " " "	No. 2.	123
" " " " " " " "	No. 4.	65
Analysis of symptoms	No. 2.	20
Anatomy, pathological	No. 2.	32
Animal experiments. <i>Baboon</i> . Abyssinian or East African disease	No. 5.	25
" " " (dog-faced) Abyssinian or East African disease	No. 6.	150
" " " (dog-faced) Jinja cattle disease	No. 6.	150
" " " " Mule disease	No. 6.	150
" " <i>Cats</i> . Bugungu dog disease	No. 8.	70
" " " Sleeping sickness	No. 6.	73
" " " " " " " "	No. 6.	94
" " <i>Chimpanzee</i> , inoculation with sleeping sickness	No. 8. {	53, 63
" " <i>Dogs</i> . Abyssinian or East Coast disease	No. 5.	24
" " " " " " " "	No. 6.	146
" " " Bugungu dog disease	No. 8.	69
" " " Entebbe ox disease	No. 5.	13
" " " Jinja cattle disease	No. 5.	18
" " " " " " " "	No. 6.	136
" " " Mule disease	No. 5.	25
" " " " " " " "	No. 5.	27
" " " " " " " "	No. 6.	147
" " " Sleeping sickness	No. 4.	37
" " " " " " " "	No. 4.	38
" " " " " " " "	No. 5.	32
" " " " " " " "	No. 6.	73
" " " " " " " "	No. 6.	90
" " " Trypanosoma fever	No. 4.	37
" " " " " " " "	No. 4.	40
" " " " " " " "	No. 5.	32
" " " Trypanosoma Gambiense in blood of	No. 8.	64

		Subject.	Report.	Page.
Animal experiments.	<i>Donkeys.</i>	Abyssinian or East African disease	No. 5.	25
" "	"	" " " " " " " " " " " "	No. 6.	162
" "	"	Bugungu dog disease	No. 8.	68
" "	"	Jinja cattle disease	No. 6.	158
" "	"	Mule disease	No. 5.	27
" "	"	" " " " " " " " " " " "	No. 6.	165
" "	"	Sleeping sickness	No. 4.	45
" "	"	" " " " " " " " " " " "	No. 6.	73
" "	"	" " " " " " " " " " " "	No. 6.	98
" "	<i>Goats.</i>	Abyssinian or East African disease	No. 5.	25
" "	"	Abyssinian and Jinja diseases	No. 6.	189
" "	"	Bugungu dog disease	No. 8.	68
" "	"	Blood, effect on trypanosomes in fly	No. 8.	132
" "	"	Jinja cattle disease	No. 5.	22
" "	"	" " " " " " " " " " " "	No. 6.	182
" "	"	Mule disease	No. 5.	27
" "	"	Mule and Jinja diseases	No. 6.	191
" "	"	Sleeping sickness	No. 4.	48
" "	"	" " " " " " " " " " " "	No. 6.	73
" "	"	" " " " " " " " " " " "	No. 6.	100
" "	<i>Guinea-pigs.</i>	Abyssinian or East African disease	No. 5.	25
" "	"	" " " " " " " " " " " "	No. 6.	152
" "	"	Bugungu dog disease	No. 8.	68
" "	"	Jinja cattle disease	No. 5.	22
" "	"	" " " " " " " " " " " "	No. 6.	150
" "	"	" " " " " " " " " " " "	No. 8.	72
" "	"	Mule disease	No. 5.	27
" "	"	" " " " " " " " " " " "	No. 6.	154
" "	"	Sleeping sickness	No. 4.	43
" "	"	" " " " " " " " " " " "	No. 6.	73
" "	"	" " " " " " " " " " " "	No. 6.	96
" "	<i>Jackall.</i>	Mule disease... ..	No. 5.	28
" "	"	" " " " " " " " " " " "	No. 6.	148
" "	"	Sleeping sickness	No. 6.	73
" "	"	" " " " " " " " " " " "	No. 6.	93
" "	<i>Monkeys.</i>	Abyssinian or East African disease	No. 5.	24
" "	"	" " " " " " " " " " " "	No. 6.	126
" "	"	Arsenic, effect of, on monkeys	No. 8.	43
" "	"	Bugungu dog disease	No. 8.	69
" "	"	Cross inoculations	No. 5.	32
" "	"	Diplo-streptococci	No. 6.	31
" "	"	Feeding fresh caught flies on	No. 1.	30
" "	"	" " " " " " " " " " " "	No. 4.	62
" "	"	" " " " " " " " " " " "	No. 5.	31
" "	"	" " " " " " " " " " " "	No. 6.	106
" "	"	Feeding stomoxys on	No. 6.	206
" "	"	Feeding tsetse flies on	No. 6.	130
" "	"	" " " " " " " " " " " "	No. 6.	199
" "	"	<i>Glossina palpalis</i> : can it convey <i>T. gambiense</i> ?	No. 6.	57
" "	"	" " " " " " " " " " " "	No. 6.	104
" "	"	<i>G. palpalis</i> : can it convey Abyssinian or East African disease?... ..	No. 6.	126
" "	"	" " " " " " " " " " " "	No. 6.	199

[illegible]

	Subject.	Report.	Page.
Bugungu, Albert Lake	No. 6.	275
"	dog disease of. <i>See under</i> Animal experiments.		
"	Sleeping sickness at	No. 6.	275
Busiro Camp, Buwanuka	No. 9.	70
Bussu Camp, Usoga	No. 9.	72
Calomel.	<i>See under</i> Drugs.		
Castellani, Aldo, found trypanosomes in sleeping sickness	No. 1.	3, 12
"	on clinical aspects of sleeping sickness	No. 2.	14
"	Development of sleeping sickness trypanosomes	No. 2.	9
"	Sleeping sickness and trypanosomes	No. 4.	4
Cases of sleeping sickness. Clinical records, tables and charts		No. 1.	39
"	" " " " " "	No. 2.	36
"	" " " " " "	No. 4.	65
"	" " " " " "	No. 6.	209
"	" " " in a Persian	No. 5.	33
"	" " " effect of drugs in	No. 8.	31
"	of Trypanosoma fever. <i>See under</i> Bara Risgallah, Jour- dien Murjan, Karala Barigi, Kumsarsabba, Tabua.		
"	" " " Case of Kitsame	No. 6.	53
"	" " " Mauawa	No. 6.	57
"	" " " " " " " " " " " "	No. 8.	29
"	" " " " " " " " " " " "	No. 6.	62
"	" " " " " " " " " " " "	No. 8.	26
"	" " " " " " " " " " " "	No. 6.	50
"	" " " " " " " " " " " "	No. 8.	28
Cats.	<i>See under</i> Animal experiments.		
Cattle.	<i>See</i> Oxen.		
Cerebro-spinal fluid.	Cells of, during life	No. 6.	25
"	" Examination of, in cases of sleeping sickness... ..	No. 1.	12
"	" Sleeping sickness: 143 lumbar punctures	No. 8.	9
"	" Trypanosomes in, of some cases of sleeping sickness	No. 1.	3
"	" Trypanosomes in, in every case of sleeping sickness	No. 4.	6
"	" Trypanosomes in, in sleeping sickness in other districts	No. 4.	6
"	" Trypanosomes not in, in other diseases	No. 4.	7
Chiggers. (Jiggers.)	Very common	No. 9.	83
Chimpanzee.	<i>See under</i> Animal experiments.		
Chinolin compounds.	<i>See under</i> Drugs.		
Christy, Cuthbert, on distribution of sleeping sickness, filaria, &c., in East Equatorial Africa	No. 2.	3
"	" on epidemiology and etiology of sleeping sickness in East Equatorial Africa	No. 3.	3
Circulatory system	No. 2.	24
"	" <i>See</i> Cases	No. 1.	39
"	" " " " " " " " " " " "	No. 2.	36
"	" " " " " " " " " " " "	No. 4.	65
Clearing of foreshores, effect of, on flies	No. 9.	34
"	open spaces and planting sweet potatoes, &c.	No. 9.	36
Climate and physical features of infective areas	No. 3.	16
Clinical features and symptoms	No. 2.	18
"	observations	No. 3.	27
"	records of a series of cases of sleeping sickness	No. 1.	39
"	" " " " " " " " " " " "	No. 2.	36
"	" " " " " " " " " " " "	No. 4.	65
"	" " " " " " " " " " " "	No. 6.	209

	Subject.	Report.	Page.
<i>Filaria nocturna</i>	No. 2.	66
" <i>perstans</i>	No. 2.	5
" "	and its relationship to sleeping sickness	No. 2.	64
" "	"	No. 3.	25
" "	Its distribution	No. 3.	25
" "	Northern limit	No. 3.	9
Fishing in the lakes and rivers to be discouraged	...	No. 9.	38
Flies.	Can other biting flies convey trypanosomata?	No. 5.	40
"	Provisional list of Diptera, sent by Col. Bruce	No. 5.	3
"	Report on collection sent by Christy	No. 3.	34
Fly areas	No. 9.	9
Fly ranges	No. 9.	9
Food.	Influence of, on sleeping sickness	No. 3.	21
" "	No. 2.	16
"	See cases	No. 1.	52
"	No. 4.	65
Food supply at the Segregation Camps	No. 9.	84
Foreshores, effect of clearing, on <i>Glossina</i>	No. 9.	34
"	suggestion that cutting timber for fuel should be restricted to	No. 9.	36
Forest, effect of clearing	No. 9.	16
General paralysis and tabes of the insane	No. 2.	35
Geographical distribution of sleeping sickness	No. 2.	15
" "	"	No. 3.	7
" "	" and history in Uganda	No. 4.	51
" "	<i>G. palpalis</i>	No. 4.	54
" "	"	No. 5.	46
" "	"	No. 6.	102
Gland juice sometimes becomes infected by bacteria	No. 6.	28
" " See cases	No. 6.	209
" punctures	No. 8.	7
Glandular enlargement.	Clinical symptoms	No. 2.	19
" "	Early records	No. 3.	5, 30
" "	In every case of sleeping sickness, and trypanosomes present	No. 6.	7
" "	In every case of trypanosoma fever, and trypanosomes present	No. 6.	12
" "	Incidence of, in general population	No. 6.	12
" "	Pathological anatomy	No. 2.	33
" "	See Cases	No. 1.	17
" "	"	No. 1.	39
" "	"	No. 2.	36
" "	"	No. 4.	65
" "	"	No. 6.	210
<i>Glossina fusca</i> .	At Lake Albert Edward	No. 9.	16
" "	Distribution	No. 6.	281
" "	Does it carry <i>T. gambiense</i> from animal to animal?	No. 8.	18
" "	Found at Kibwesi, British East Africa	No. 5.	5
" "	" " " " " "	No. 5.	45
" "	Found at Lake Rudolph	No. 6.	112
" <i>longipalpis</i> .	Distribution	No. 6.	281
" <i>morsitans</i> .	Distribution	No. 6.	280
" "	" in Northern Uganda	No. 9.	9
" "	Found in Bahr-el-Ghazal	No. 6.	275
" <i>pallidipes</i> .	Found at Igagas, &c.	No. 5.	14
" "	" " " " " "	No. 6.	111
" <i>palpalis</i> .	Anatomy of	No. 8.	106
" "	Artificially infected with <i>T. gambiense</i>	No. 8.	124

Subject.		Report.	Page
<i>Glossina palpalis</i> .	Measures for reducing the number of	No. 9.	40
" "	Methods for extermination of	No. 9.	29
" "	Multiplication of trypanosomes in fly	No. 6.	282
" "	Natural range of	No. 9.	17
" "	Numerical proportions of male and female	No. 9.	15
" "	Only small percentage of flies in an infected area carry infection	No. 9.	31
" "	Pupa of	No. 6.	209
" "	" discovered in natural breeding grounds	No. 9.	48
" "	Proportion of freshly caught flies that contain trypanosomes	No. 6.	284
" "	Range of fly from water is far narrower than was supposed	No. 9.	28
" "	Working knowledge of habits of fly	No. 9.	5
" <i>tachinoides</i> .	Distribution	No. 6.	281
Goats.	See under Animal experiments.		
Gray, Lieut. (now Capt.) A. C. H.	Continuation report	No. 6.	5
" "	Continuation report on sleeping sickness	No. 8.	3
" "	On multiplication of <i>T. gambiense</i> in <i>G. palpalis</i>	No. 6.	282
" "	Report on the sleeping sickness camps, Uganda, &c.	No. 9.	62
" "	Further report on the treatment of sleeping sickness patients, &c.	No. 9.	86
Greig, Capt. E. D. W.	Report by	No. 4.	1
" "	Further observations, &c.	No. 5.	8
" "	In British East Africa...	No. 5.	45
" "	Report by	No. 6.	5
" "	Sleeping sickness in the Nile valley	No. 6.	273
Guinea-pig.	See under Animal experiments.		
Hæmapoietic system		No. 2.	31
Hodges, Dr. A. D. P.	Distribution of sleeping sickness	No. 4.	51
" "	First half-yearly report of the Medical Officer in Charge of the Sleeping Sickness Extended Investigations, &c. (Summary at p. 43)	No. 9.	4
" "	Progress of sleeping sickness epidemic	No. 3.	19
" "	Report on sleeping sickness in Unyoro and Nile valley	No. 8.	86
" "	Spirochæta fever	No. 5.	9
" "	Sleeping sickness epidemic on the Nile bank—between Nimule and Wadelai	No. 9.	21
Immunity of race from sleeping sickness		No. 3.	25
Incubation period of sleeping sickness		No. 2.	32
" "		No. 3.	27
" "		No. 4.	65
Infective localities, characteristics of		No. 3.	16
" "	what constitutos	No. 9.	6
Insects.	Blood-sucking maggot	No. 6.	275
"	Diptera, a provisional list of	No. 5.	3
"	Does sleeping sickness coincide with distribution of any biting insect?	No. 1.	36
"	"	No. 4.	52
" Jiggers (Chiggers).	" See cases	No. 4.	70
"	"	No. 6.	210
"	Very common in camp	No. 9.	83

Subject.								Report.	Page.
Insects.	Lice.	Very common in camp						No. 9.	83
"		Report on mosquitoes and flies by Theobald						No. 3.	33
"	Ticks.	<i>Ornithodoros moubata</i> , &c.						No. 5.	6
"	"	" "							

[illegible]

Subject.						Report.	Page.
Nile.	Presence of flaria in the Upper Nile districts	No. 2.	66
"	Presence of sleeping sickness on the Nile	No. 6.	276
"	" " " " " "	No. 8.	87
"	Presence of tsetse flies on the Nile	No. 4.	54
"	" " " " " "	No. 5.	47
"	" " " " " "	No. 6.	275
"	Sleeping sickness. Epidemic at two places between Wadelai and Nimule	No. 9.	7
Nitro phenyl arsenic acid. <i>See under</i> Drugs.							
Occupation, influence of, on sleeping sickness							
Oxen.	<i>See under</i> Animal Experiments.	No. 3.	20
Parasites.	<i>Ankylostoma duodenale</i>	No. 2.	16
"	" " Presence in dogs	No. 4.	37
"	" " " " " "	No. 8.	65
"	" " " " Presence in sleeping sickness cases	No. 2.	69
"	" " " " <i>See cases</i>	No. 1.	39
"	" " " " " "	No. 2.	36
"	Bacteria. <i>Streptococcus</i>	No. 1.	10
"	" " " " " "	No. 2.	17
"	" " " " " "	No. 5.	22
"	Filaria in monkeys. New species	No. 5.	22
"	" in dogs	No. 8.	70
"	" <i>demarquaii</i>	No. 2.	66
"	" <i>nocturna</i>	No. 2.	66
"	" <i>perstans</i>	No. 2.	5
"	" " " " " "	No. 2.	16
"	" " " " " "	No. 2.	64
"	" " " " " "	No. 3.	9
"	Hæmagregarine in the blood of crocodiles	No. 8.	131
"	Halteridia in the blood of birds	No. 8.	131
"	Herpetomonas in house fly	No. 8.	131
"	" " in stomoxys	No. 8.	133
"	Malaria in monkeys	No. 1.	29
"	<i>Piroplasmosis canis</i>	No. 5.	32
"	<i>Plasmodium kochi</i>	No. 8.	84
"	<i>Rhabdonema strongyloides</i>	No. 2.	16
"	Spirochæta. Tick fever in Man	No. 5.	33
"	" " " " " "	No. 8.	97
"	<i>Strongylus armatus</i> in zebras	No. 8.	84
"	<i>Tenia solum</i> in dogs	No. 8.	65
"	Trypanosomes—Abyssinian or East African	No. 5.	22
"	" Bugungu dog	No. 8.	64
"	" Entebbe ox	No. 4.	47
"	" <i>Grayi</i> of tsetse flies	No. 8.	122
"	" Jinga cattle	No. 5.	14
"	" Mule	No. 5.	27
"	" Sleeping sickness	No. 1.	3
"	" Trypanosoma fever	No. 1.	9
"	" <i>Tullocki</i>	No. 8.	122
"	" <i>See also under</i> Trypanosomes and Glossina.		
Paratolylarsenic acid. <i>See under</i> Drugs.							
Pathological anatomy of sleeping sickness						No. 2.	32
Physical features and climate of infective areas						No. 3.	16
Piroplasmosis in dogs						No. 5.	32
"	" " " " " "	No. 5.	36
"	" in monkeys	No. 8.	84

Subject.							Report.	Page.
Plague in Budu	No. 3.	31
"	"	"	"	"	"	"	No. 8.	97
<i>Plasmodium kochi</i> in monkeys	No. 8.	84
Plimmer, Dr. H. G., and Dr. J. D. Thomson.	Preliminary summary of the results of the experimental treatment of trypanosomiasis in rats						No. 9.	97
"	"	"	"	"	"	"	No. 9.	107
Plimmer, R. H. Aders.	Note upon sodium antimonyl tartrate						No. 9.	117
Polyadenitis.	In early stages	No. 6.	25
"	Lymphatic system...	No. 2.	28
"	Most constant lesion	No. 6.	67
"	Sleeping sickness is characterised by a chronic polyadenitis						No. 7.	6
Post mortem examinations of animals	No. 5.	13
"	"	"	No. 6.	74
"	"	Monkeys	No. 4.	24
"	"	See cases	No. 1.	39
"	"	"	No. 4.	65
"	"	"	No. 6.	49
"	"	"	No. 6.	209
"	"	Sleeping sickness.	Analyses of	No. 8.	16
Potassium antimonyl tartrate.	See under Drugs.							
Precautionary and preventive measures	No. 8.	93
Predisposing causes of sleeping sickness	No. 9.	25
Premonitory symptoms of sleeping sickness	No. 2.	18
Prime Minister, Uganda, on area of sleeping sickness	No. 3.	27
"	"	Meets the Commission	No. 4.	52
"	"	On hut tax labour	No. 1.	38
Prognosis of sleeping sickness	No. 2.	35
Propagation characteristics of sleeping sickness...	No. 3.	22
Protection of natives in rubber collecting	No. 9.	37
Rabbits.	See under Animal Experiments.							
Race, immunity of, from sleeping sickness	No. 4.	65
Rats.	See under Animal Experiments.							
Regents, Uganda.	Visit laboratory	No. 1.	36
"	"	"	No. 4.	52
Re-injections into animals...	No. 5.	31
Re-inoculations and cross inoculations with human blood and cerebro-spinal trypanosomes	No. 5.	32
Removal of dwellings, markets, &c, out of fly range	No. 9.	36
Reports of Royal Society's Commission on Sleeping Sickness—								
"	Part 1.	Presence of trypanosomes in sleeping sickness.	Castellani	No. 1.	3
"	"	2.	Progress, on sleeping sickness in Uganda.	Bruce and Nabarro	No. 1.	11
"	"	3.	Distribution of sleeping sickness and filaria, &c.	Christy	No. 2.	3
"	"	4.	Form of trypanosomes in sleeping sickness.	Castellani	No. 2.	9
"	"	5.	Sleeping sickness from its clinical aspect.	Low and Castellani	No. 2.	14
"	"	6.	Epidemiology and etiology of sleeping sickness.	Christy	No. 3.	3

	Subject.	Report.	Page.
Reports of Royal Society's Commission on Sleeping Sickness—			
"	Part 7. Mosquitoes and flies collected by Christy.		
"	Theobald	No. 3.	33
"	8. Further, on sleeping sickness in Uganda.		
"	Bruce, Nabarro, and Greig	No. 4.	3
"	9. A provisional list of diptera. Austen ...	No. 5.	3
"	10. Further observations on trypanosomiasis.		
"	Nabarro and Greig	No. 5.	8
"	11. Sleeping sickness in Uganda. Greig and		
"	Gray	No. 6.	1
"	12. Sleeping sickness in the Nile valley.		
"	Greig	No. 6.	273
"	13. Distribution of tsetse flies. Austen ...	No. 6.	278
"	14. Multiplication of trypanosomes in flies.		
"	Gray and Tulloch	No. 6.	282
"	15. Histological observations on sleeping sick-		
"	ness, &c. Mott	No. 7.	5
"	16. Continuation, of sleeping sickness in		
"	Uganda. Gray and Tulloch	No. 8.	3
"	17. Experiments with tsetse flies. Ross ...	No. 8.	80
"	18. Sleeping sickness in Unyoro and the Nile		
"	valley. Hodges	No. 8.	86
"	19. Tour of Mr. Speke and Dr. Adams.		
"	Adams	No. 8.	100
"	20. Anatomy of <i>G. palpalis</i> Minchin ...	No. 8.	106
"	21. <i>G. palpalis</i> in relation to <i>T. gambiense</i>		
"	and other trypanosomes. Minchin,		
"	Gray, and Tulloch	No. 8.	122
"	22. Eneystation in <i>T. grayi</i> . Minchin ...	No. 8.	137
"	23. Sleeping sickness in Uganda from Jan. 1st		
"	to June 30th, 1906. Hodges	No. 9.	4
"	24. Sleeping sickness camps, Uganda, and		
"	medical treatment of sleeping sickness		
"	patients, from Dec., 1906, to Jan., 1908.		
"	Gray	No. 9.	62
"	25. Preliminary summary of the results of the		
"	experimental treatment of trypanoso-		
"	miasis in rats. Plimmer and Thomson	No. 9.	97
"	26. Further results of the experimental treat-		
"	ment of trypanosomiasis in rats.		
"	Plimmer and Thomson	No. 9.	107
"	27. Note upon sodium antimonyl tartrate.		
"	Plimmer (R. H. A.)	No. 9.	117
Respiratory system in sleeping sickness		No. 2.	27
"	" " " " See cases	No. 1.	39
"	" " " " " "	No. 2.	36
"	" " " " " "	No. 4.	65
"	" " " " " "	No. 9.	8
"Ruhinyo," an epidemic disease in Uganda			
Scrub and forest, effect of clearing		No. 9.	16
Seasons, influence of, in sleeping sickness		No. 3.	21
Segregation of sleeping sickness patients		No. 9.	7
"	"		50
"	"		86
"	camps—Busiro Camp—Buwanuka... ..	No. 9.	70
"	" Bussu Camp—Usoga	No. 9.	72
"	" Detailed account of	No. 9.	70
"	" Food supply at	No. 9.	84
"	" Kyetume Camp, Chagwe	No. 9.	72
Sese Islands, examination of natives for sleeping sickness in ...		No. 8.	9
"	Filaria in	No. 2.	64

	Subject.	Report.	Page.
Tables.	Incidence of trypanosomes in blood of general population in non-sleeping sickness area	No. 4.	16
"	" " " " " "	No. 4.	14
"	Injection of different trypanosomes into animals ...	No. 6.	195
"	Nagana rats treated with atoxyl and succinimide of mercury	No. 9.	101
"	Nagana and Surra rats treated with Donovan's solution and atoxyl ...	No. 9.	104
"	" " " " atoxyl and iodipin	No. 9.	104
"	" " " " atoxyl and lactate of mercury ...	No. 9.	103
"	" " " " atoxyl and mercury sozoiodol ...	No. 9.	103
"	" " " " sodium antimonyl tartrate ...	No. 9.	114
"	Number and present condition of patients treated with atoxyl and mercury, and mercury alone ...	No. 9.	93
"	Number of patients, type of case on admission, sex, system of treatment, &c., &c.	No. 9.	96
"	Number of sleeping sickness patients who presented certain symptoms possibly due to atoxyl	No. 9.	96
"	<i>Post-mortem</i> examinations for trypanosomes... ..	No. 8.	18
"	Present condition of patients admitted during the four different quarters of the year 1907	No. 9.	91
"	Sleeping sickness on the Nile as far north as Wadelai ...	No. 6.	276
"	Surra rats treated with atoxyl and succinimide of mercury, &c.	No. 9.	102
"	" " " " " "	No. 9.	108
"	Summary of results obtained "with atoxyl"-proof strains of Nagana and Surra in rats	No. 9.	106
"	Trypanosomes in blood by day and by night... ..	No. 6.	25
"	Trypanosomiasis, animal	No. 5.	15
Tabula,	trypanosoma fever in the case of	No. 1.	21
"	" " " " " "	No. 4.	12
"	" " " " Apparently in good health	No. 5.	29
"	" " " " Cerebro-spinal fluid contains trypanosomes	No. 6.	39
"	" " " " Examination of brain	No. 7.	32
"	" " " " Further notes on case	No. 8.	15
"	" " " " Further note on case and death	No. 8.	19
Tragaroth. <i>See under</i> Drugs.			
Trypanosoma fever. <i>See under</i> Animal Experiments.			
"	" Can any difference be made out between sleeping sickness and trypanosoma fever microscopically or by experiment?	No. 1. {	9
			24
			25
"	" Cases. Mauawa	No. 8.	29
"	" " Mondu. Case and death	No. 8.	26
"	" " Tenwa	No. 8.	28
"	" <i>See under</i> Bara Risgallah, Jourdien Murjan, Karala Barigi, Kumsarsabba, Tabula.		
"	" Gland enlargement in	No. 6.	12
"	" Has it any connection with sleeping sickness?	No. 4.	7
"	" " " " " "	No. 6.	39
"	" Its relation to sleeping sickness	No. 8.	18

	Subject.	Report.	Page.
Trypanosoma fever.	Microscopically, no difference between the trypanosome of, and that of sleeping sickness	No. 4.	20
Trypanosomes, in Abyssinian or East African disease...	No. 5.	22
"	" " " " animals affected	No. 6.	111
"	Adult and development forms of trypanosomes	No. 2.	9
"	Are other varieties of trypanosomes found in Uganda?	No. 6.	111
"	Are other trypanosomes pathogenic to animals?	No. 6.	112
"	Are the trypanosomes of sleeping sickness and trypanosoma fever pathogenic to animals?	No. 4.	20
"	Are we dealing with one or more species? ...	No. 4.	50
"	" " " " " " ...	No. 6.	193
"	Bugungu dog disease	No. 8.	64
"	Can trypanosomes travel from intestine to salivary gland of tsetse flies?	No. 6.	287
"	<i>T. Castellani</i>	No. 1.	10
"	Cerebro-spinal fluid of all sleeping sickness cases contains trypanosomes	No. 4.	6
"	Cerebro-spinal fluid of other diseases does not contain trypanosomes	No. 4.	7
"	Cultivation of <i>T. gambiense</i>	No. 8.	133
"	Distribution of trypanosomes in Uganda and British East Africa	No. 6.	111
"	Encystation of <i>T. grayi</i> , &c.	No. 8.	137
"	Experiments by Dr. Wiggins	No. 5.	46
"	Gland puncture in cases of sleeping sickness. Trypanosomes always present	No. 6.	7
"	<i>T. Grayi</i> . Description... ..	No. 8.	123
"	History and distribution of	No. 6.	111
"	Histological observations on	No. 7.	3
"	In animals	No. 8.	98
"	Incidence of, in blood of general population in British East Africa	No. 4.	19
"	Inoculation of contents of fly	No. 6.	286
"	In sick mule, Entebbe	No. 5.	25
"	Is there a specific carrier for each variety of trypanosome?	No. 5.	38
"	In Jinja cattle disease	No. 5.	14
"	" " " " Action of trypanosome of, on animals	No. 6.	112
"	" " " " Inoculations and effect of drugs on... ..	No. 8.	71
"	" " " " Morphology and pathogenicity of trypanosome of for animals	No. 5.	18
"	Microscopical difference in trypanosomes	No. 6.	112
"	More numerous at night than day	No. 6.	25
"	Morphology of trypanosomes seen in fly	No. 6.	284
"	Mule disease. Its action on animals... ..	No. 6.	113
"	Multiplication of, in <i>G. palpalis</i>	No. 6.	282
"	No difference microscopically between sleeping sickness and trypanosoma fever trypanosomes	No. 4.	20
"	Of ox disease, Entebbe	No. 5.	11
"	" " " " Action on animals	No. 6.	112
"	Production of an atoxyl-proof race of, in rats	No. 9.	105

	Subject.	Report.	Page.
Trypanosomes.	In Sleeping sickness, first observation of ...	No. 1.	3
"	" experiments on monkeys with cerebro-spinal fluid from cases of ...	No. 4.	21
"	" Is it conveyed by tsetse flies of British East Africa? ...	No. 5.	45
"	" Identity of trypanosoma of, with <i>T. gambiense</i> ...	No. 8.	53
Trypanroth.	<i>See under Drugs.</i>		
Tsetse flies.	Distribution of ...	No. 6.	278
"	<i>See under Glossina.</i>		
Tulloch, Lieutenant.	Multiplication of <i>T. gambiense</i> in <i>G. palpalis</i> ...	No. 6.	282
"	" Continuation report on sleeping sickness in Uganda ...	No. 8.	3
"	" On relation of <i>G. palpalis</i> to <i>T. gambiense</i> ...	No. 8.	122
Tumours and intercranial syphilis, &c.	No. 2.	35
Uffman, Dr.	Arrived Entebbe, February 5th, 1906 ...	No. 9.	4
Unyoro. Filaria in	No. 2.	66
"	Sleeping sickness in northern Unyoro and Victoria Nile ...	No. 8.	100
"	" " in Unyoro and Nile valley ...	No. 8.	86
Urinary system in sleeping sickness	No. 2.	30
Van Someran.	Arrived at Entebbe, February 5th, 1906, and proceeded to Kampala ...	No. 9.	4
Weatherhead, Mr.	Examination of Sese natives by ...	No. 8.	9
Wiggins, Dr.,	notes absence of filaria in sleeping sickness cases in Kavirondo ...	No. 2.	65
"	On conveyance of sleeping sickness by East African tsetse flies ...	No. 5.	45
"	His journey to Shirati and conclusions therefrom ...	No. 6.	103
"	Observes trypanosomes in sleeping sickness cases at Kisumu ...	No. 1.	14
"	Usoga assigned to, as his sphere ...	No. 9.	4
"	On range of tsetse flies ...	No. 9.	18
Wild animals, blood of, examined.	Coke's hartebeest... ..	No. 8.	84
"	" " Hippopotami ...	No. 8.	130
"	" " Mpala ...	No. 8.	84
"	" " Thomson's gazelle ...	No. 8.	84
"	" " Zebra ...	No. 8.	84
"	" " Aquatic birds ...	No. 8.	130
"	" " Crocodiles ...	No. 8.	131
"	blood of, sucked by flies. Chameleons ...	No. 8.	131
"	" " Lizards ...	No. 8.	131
"	" " Snakes ...	No. 8.	131
Will, Lieut.-Col. J., R.A.M.C.	Introduction to Dr. Hodges' Report of the Sleeping Sickness Extended Investigations in Uganda ...	No. 9.	3

REPORTS
OF THE
SLEEPING SICKNESS COMMISSION
OF THE
ROYAL SOCIETY.

No. X.

LONDON:
PRINTED FOR HIS MAJESTY'S STATIONERY OFFICE,
By DARLING & SON, LTD., 34-40, BACON STREET, E.

And to be purchased, either directly or through any Bookseller, from
WYMAN AND SONS, LTD., FETTER LANE, E.C.; or
OLIVER & BOYD, TWEEDDALE COURT, EDINBURGH; or
E. PONSONBY, 116, GRAFTON STREET, DUBLIN.

1910.

Price Three Shillings.



REPORTS

OF THE

SLEEPING SICKNESS COMMISSION

OF THE

ROYAL SOCIETY.

No. X.

LONDON:
PRINTED FOR HIS MAJESTY'S STATIONERY OFFICE,
By DARLING & SON, LTD., 34-40, BACON STREET, E.

And to be purchased, either directly or through any Bookseller, from
WYMAN AND SONS, LTD., FETTER LANE, E.C.; or
OLIVER & BOYD, TWEEDDALE COURT, EDINBURGH; or
E. PONSONBY, 116, GRAFTON STREET, DUBLIN.

1910.

Price Three Shillings.

CONTENTS.

	PAGE
29. Further Results of the Experimental Treatment of Trypanosomiasis : being a Progress Report to a Committee of the Royal Society. By H. G. Plimmer, F.L.S., and H. R. Bateman, Captain R.A.M.C. ...	3
30. A Trypanosome from Zanzibar. By Colonel Sir David Bruce, C.B., M.B., F.R.S., D.Sc., LL.D., Army Medical Service, and Captains A. E. Hamerton, D.S.O., and H. R. Bateman, Royal Army Medical Corps	12
31. Trypanosoma Ingens, n. sp. By Colonel Sir David Bruce, C.B., F.R.S., Army Medical Service ; Captains A. E. Hamerton, D.S.O., and H. R. Bateman, Royal Army Medical Corps ; and Captain F. P. Mackie, Indian Medical Service	27
32. Further Results of the Experimental Treatment of Trypanosomiasis : being a Progress Report to a Committee of the Royal Society. By H. G. Plimmer, F.L.S., and W. B. Fry, Captain R.A.M.C. ...	29
33. The Development of Trypanosoma Gambiense in Glossina Palpalis. By Colonel Sir David Bruce, C.B., F.R.S., Army Medical Service ; Captains A. E. Hamerton, D.S.O., and H. R. Bateman, Royal Army Medical Corps ; and Captain F. P. Mackie, Indian Medical Service. (Sleeping Sickness Commission of the Royal Society, 1908-09)	46
34. A Note on the Occurrence of a Trypanosome in the African Elephant. By Colonel Sir David Bruce, C.B., F.R.S., Army Medical Service ; Captains A. E. Hamerton, D.S.O., and H. R. Bateman, Royal Army Medical Corps ; and Captain F. P. Mackie, Indian Medical Service. (Sleeping Sickness Commission of the Royal Society, 1908-09)	54
35. Sleeping Sickness in Uganda.—Duration of the Infectivity of the Glossina Palpalis after the Removal of the Lake-shore Population. By Colonel Sir David Bruce, C.B., F.R.S., Army Medical Service ; Captains A. E. Hamerton, D.S.O., and H. R. Bateman, Royal Army Medical Corps ; and Captain F. P. Mackie, Indian Medical Service. (Sleeping Sickness Commission of the Royal Society, 1908-09)	56
36. Glossina Palpalis as a Carrier of Trypanosoma Vivax in Uganda. By Colonel Sir David Bruce, C.B., F.R.S., Army Medical Service ; Captains A. E. Hamerton, D.S.O., and H. R. Bateman, Royal Army Medical Corps ; and Captain F. P. Mackie, Indian Medical Service. (Sleeping Sickness Commission of the Royal Society, 1908-09)	63
37. On the Action of Antimony Compounds in Trypanosomiasis in Rats : being a Report to a Sub-Committee of the Tropical Diseases Committee of the Royal Society. By John D. Thomson, M.B., C.M., and Arthur R. Cushny, M.D., F.R.S.	67
38. Report on a Collection of Blood-Parasites made by the Sleeping Sick- ness Commission, 1908-9, in Uganda. By E. A. Minchin, M.A., Professor of Protozoology in the University of London	73
39. Amakebe : a Disease of Calves in Uganda. By Colonel Sir David Bruce, C.B., F.R.S., Army Medical Service ; Captains A. E. Hamerton, D.S.O., and H. R. Bateman, Royal Army Medical Corps ; and Captain F. P. Mackie, Indian Medical Service. (Sleeping Sickness Commission of the Royal Society, 1908-09) ...	86

[Reprinted from the PROCEEDINGS OF THE ROYAL SOCIETY,
B. Vol. 80.]

29. FURTHER RESULTS OF THE EXPERIMENTAL
TREATMENT OF TRYPANOSOMIASIS: BEING A
PROGRESS REPORT TO A COMMITTEE OF THE
ROYAL SOCIETY.

By H. G. PLIMMER, F.L.S., and H. R. BATEMAN, Captain
R.A.M.C.

(Communicated by J. Rose Bradford, M.D., F.R.S. Received
August 25th, 1908.)

The following results are a continuation of the work of which
summaries have already appeared in the "Proceedings of the
Royal Society."*

The experiments have been carried out with the same strains
of Nagana and Surra as were used before.

A.—*Condition of the Animals living at the Date of the Com-
pletion of the Tables in the last Paper.*

*Table I.—Nagana Rats treated with Atoxyl and Succinimide of
Mercury.*

(Average duration of untreated disease, 5·5 days.)

No. 4 died on the 307th day after inoculation.

" 7	" 365th	"
" 10	" 249th	"
" 15	" 188th	"
" 21	" 63rd	"

Of these, No. 15, which was apparently cured, was used on the
147th day after inoculation for re-inoculation, with the view of
ascertaining if any immunity had been conferred. This was
found not to be the case.†

None of the above died with any of the signs of Nagana. Of
the 21 rats tabulated,‡ only one died from trypanosomiasis, and
this one was probably atoxyl-proof.

*Table III.—Surra Rats treated with Atoxyl and Mercury
Sozoiodol.*

No. 5 died on the 286th day after inoculation from broncho-
pneumonia.

Table VI.—Surra Rats treated with Atoxyl and Iodopin.

No. 9 died on the 221st day after inoculation from worms.

* B, vol. 79, 1907, pp. 505–516, and B, vol. 80, 1908, pp. 1–12.

† *Vide* 'Roy. Soc. Proc.,' B, vol. 80, p. 10.

‡ 'Roy. Soc. Proc.,' B, vol. 79, p. 510.

Rats treated with Atoxyl and Liq. Hydrarg. Perchlor.

The rat still living at the date of the last paper died on the 187th day after inoculation from broncho-pneumonia.

Rats treated with Sodium Antimonyl Tartrate. (Table on pp. 8—9 of the last Paper.) Results to August 20.*

No.	7	is living and well 354 days after inoculation.		
"	8	died on the	194th day	"
"	9	"	323rd	"
"	10	"	145th	"
"	14	"	48th	"
"	15	"	67th	"
"	16	"	227th	"
"	17	"	227th	"
"	19	"	161st	"
"	20	"	49th	"
"	21	"	210th	"
"	23	"	104th	"
"	25	"	134th	"
"	26	"	134th	"
"	27	"	33rd	"
"	28	"	34th	"
"	29	"	57th	"
"	30	"	28th	"
"	31	"	147th	"
"	32	is living and well 346 days after inoculation.		
"	33	died on the	228th day	"
"	34	"	188th	"
"	35	is living and well 346 days after inoculation.		
"	36	died on the	228th day	"
"	38	"	173rd	"

It will be noticed that nine of the above rats lived for over 200 days, and nine others considerably over 100 days. Of those which have died only four have had recurrences (two had one, and two had three recurrences); none of them died with any symptoms of trypanosomiasis, and in none were trypanosomes found after death. An emulsion of the liver and of the bone-marrow of Nos. 9, 16, 17, 21, and 25 was injected into other rats with negative results in every case.

Rats treated with equal parts of 1 per cent. Solutions of Sodium Antimonyl Tartrate and Sodium Arsenyl Tartrate.

The five rats living at the date of the last paper have died:—

No.	1	died on the 199th day after inoculation.		
"	2	"	26th	"
"	3	"	43rd	"
"	4	"	59th	"
"	5	"	40th	"

As was anticipated from the earlier experiments, this treatment has no advantages over that with antimony alone.

B.—*Further Experiments.**Potassium Antimonate.*

This was tried in doses up to 7 minims of a 1 per cent. solution. In this dose it was poisonous to rats, and it did not kill the trypanosomes.

Atoxyl and Sodium Antimonyl Tartrate.

This was given in doses of 5—7 minims of a 5 per cent. solution of atoxyl and of a 1 per cent. solution of sodium antimonyl tartrate. Three Nagana rats lived respectively 23, 43, and 41 days; they all had recurrences (the last had five) and died with living trypanosomes in the blood.

Pushing the drug does not have any good effect (*see* next table); the trypanosomes are not driven out more quickly, or more effectually; recurrences are more common, and inflammatory intestinal lesions were present in nearly every case. Two rats died with living trypanosomes in the blood: these two had become antimony-proof, as the later doses did not remove the trypanosomes from the blood, nor make any difference in their number. This strain did not maintain this quality for long, as after the second sub-inoculation from these rats the trypanosomes seemed to have become normal in their behaviour towards anti-mony. The strain was lost at this point.

Nagana Rats treated with Large Doses of Sodium Antimonyl Tartrate.

No.	Weight in Grammes.	Total Quantity of 1 per cent. sod. ant. tart. given, in c.o.	Recur- rences.	Results.
1	200	5.75	1	Died on 30th day with intestinal lesions.
2	125	5.0	0	Died on 34th day with very marked intestinal lesions.
3	100	4.75	0	Died on 24th day: intestines necrotic.
4	100	4.0	0	Died on 108th day from pneumonia.
5	110	4.9	1	Died on 43rd day with inflamed intestines.
6	110	6.5	2	Died on 38th day with necrotic intestines.
7	175	8.5	2	Died on 40th day: trypanosomes in blood at death; paralysed.
8	110	9.0	2	Died on 45th day in similar condition to No. 7.
9	150	5.0	4	Died on 73rd day from gangrene of tail.
10	175	5.25	1	Died on 64th day from pneumonia.

Rats treated with Sodium Antimonyl Tartrate after Inoculation with Atoxyl-proof Trypanosomes.

The rats in the following table were all treated firstly with atoxyl to make sure that they were atoxyl-proof, and the treatment with antimony was then begun, when the trypanosomes were in large numbers in the blood.

—	No.	Weight in Grammes.	Total Quantity of 1 per cent. sod. ant. tart. given, in c.c.	Recur- rences.	Results.
Na- gana.	1	100	3.0	1	Died on 29th day with trypano- somes in blood.
	2	100	1.0	0	Died on 11th day from nephritis.
	3	110	3.0	1	Died on 54th day.
	4	110	3.0	1	Died on 20th day with trypano- somes in blood.
Surra	5	175	3.0	0	Died on 117th day from broncho- pneumonia.
	6	100	3.0	0	Died on 27th day from septi- cæmia.
	7	145	5.75	1	Died on 41st day from pneumonia.
	8	140	4.0	1	Died on 38th day with trypano- somes in blood.

It will be seen that the atoxyl-proof strains of trypanosomes are less influenced by antimony than are the ordinary variety, as three of the above rats had living trypanosomes in the blood at death, and seven of them died at a very early date.

Rats treated with Antimony (Metal) and Sodium Antimonyl Tartrate suspended in a Fatty Medium.

Sodium antimonyl tartrate, when injected in watery solution into man produces very severe pain and inflammation in the neighbourhood of the injection, with more or less local necrosis. In order to make the use of antimony practicable in the form of injection, a series of experiments was undertaken, using various other media than water for solution or suspension of the antimony salt. Lanolin, olive oil, and sesamum oil were tried, but the results were not good. Finally, the medium Colonel Lambkin devised,* consisting of palmitin and antiseptics, which is used very largely for the intramuscular injection of calomel and mercury in syphilis, was tried, with the results which are set forth in the tables below.

One great advantage of these preparations is that they can be used upon man with far less difficulties and after-consequences than the watery solutions, which seem to be impracticable; this is of importance should antimony be found of use in human trypanosomiasis.

Major Ward, R.A.M.C., has used both the forms mentioned above on men for other purposes, and he has very kindly placed his notes at our disposal. In one of his cases four doses of $\frac{1}{2}$ grain of sodium antimonyl tartrate, suspended in Colonel Lambkin's medium, were given intramuscularly into the buttock, the intervals between the doses being 3, 4, and 3 days: the doses were then increased to 1 grain, and seven doses of this strength were given, the intervals being 4, 3, 2, 4, 2, and 13 days. In all, this patient had 9 grains of the salt. Major Ward says that "the injections caused a certain amount of tenderness and discomfort at the seat of injection," but that is very different to the effects noticed after the injection of the watery solution.

Major Ward also treated two patients with antimony itself

* 'Journ. Roy. Army Med. Corps,' 1906.

in a state of extremely fine division suspended in Colonel Lambkin's medium; they were each given one dose of 1 grain, and 11 days afterwards $\frac{1}{2}$ grain. This form caused both pain and discomfort, and also a general increase in the size of the buttock, into which the injection was made, but this subsided without suppuration. This form would appear, however, to be much the more powerful of the two, as the effects obtained from the $1\frac{1}{2}$ grains of the metal were as good and as lasting as those observed in the case in which 9 grains of sodium antimonyl tartrate were given.

The following tables show the results obtained in rats with sodium antimonyl tartrate and antimony prepared as mentioned above:—

Sodium Antimonyl Tartrate, 5 per cent., in Colonel Lambkin's Medium.

—	No.	Weight in Grammes.	No. of Doses given.	Total Quantity given, in Minims.	Recur- rences.	Results to August 20.
Na- gana.	1	100	4	18	2	Died on 53rd day : bad itch.
	2	100	2	6	1	Died on 16th day with intestinal lesions.
	3	115	1	2	0	Died on 113th day of pneumonia.
	4	150	1	2	0	Died on 19th day of pneumonia.
	5	110	5	17	1	Died on 27th day : abscess.
	6	125	3	13	0	Died on 26th day of pneumonia.
	7	150	3	13	0	Died on 89th day : itch.
	8	175	1	3	1	Died on 24th day : abscess.
	9	200	3	17	1	Died on 40th day of injury.
	10	225	3	13	2	Died on 28th day with intestinal lesions.
Surra	11	115	2	6	1	Died on 22nd day of pneumonia.
	12	220	11	33	7	Died on 66th day with acute intestinal lesions.
	13	125	1	3	0	<i>Living and well 154 days after inoculation.</i>

None of the above have died from trypanosomiasis. In rats the intra-muscular injection of even a few minims is difficult, and if any of the material be left under the skin a slough forms, which takes a long time to heal. It will be noticed that No. 3 had only one dose: the rat lived 113 days and died of pneumonia; inoculations made from its organs were negative. No. 13, which is still living (154 days), has also had only one dose.

From the following table it will be seen that the administration of the metal itself has a considerable effect on the trypanosomes: it has a distinctly better effect on Surra than upon Nagana, four Surra rats out of 16 being still alive, and four others having lived for a long time. In none of the Surra rats were trypanosomes found at death, whereas in three of the Nagana rats they were present. The metal is much more irritating than the tartrate, but the effect is in most cases more prolonged; this is probably due to the fact that the absorption of the metal is much slower. Further, the smaller doses would appear to be the most efficient.

Antimony, in a state of very fine division, 5 per cent., in Colonel Lambkin's Medium.

—	No.	Weight in Grammes.	No. of Doses given.	Total Quantity given, in Minims.	Recur- rences.	Results to August 20.
Na- gana.	1	100	3	12	3	Died on 61st day : abscess.
	2	200	3	11	2	Died on 29th day with trypano- somes in blood.
	3	100	3	9	1	Died on 34th day with intestinal lesions.
	4	110	3	12	1	Died on 15th day with trypano- somes in blood.
	5	100	4	14	1	Died on 27th day with intestinal lesions.
	6	150	4	15	2	Died on 26th day with intestinal lesions.
	7	150	6	23	3	Died on 33rd day with trypano- somes in blood.
	8	300	3	13	4	Died on 51st day from broncho- pneumonia.
	9	300	2	8	2	Died on 36th day from broncho- pneumonia.
	10	200	2	8	0	<i>Living and well 204 days after inoculation.</i>
	11	300	2	8	1	Died on 29th day : abscess.
	12	250	2	8	1	Died on 39th day from broncho- pneumonia.
	13	250	2	8	7	Died on 92nd day from pneu- monia.
	14	300	1	5	0	Died on 32nd day : fatty liver.
	15	300	1	5	0	Died on 30th day.
	16	150	1	3	0	Died on 74th day from pneu- monia.
Surra	17	110	1	5	0	<i>Living and well 230 days after inoculation.</i>
	18	125	4	17	4	Died on 146th day : one recur- rence took place after an in- terval of 12 weeks.
	19	250	4	35	3	Died on 48th day from broncho- pneumonia.
	20	225	1	4	0	Died on 39th day from broncho- pneumonia.
	21	100	1	4	0	Died on 44th day : itch.
	22	100	3	10	1	Died on 44th day : itch.
	23	150	2	9	1	Died on 216th day of pneumonia.
	24	100	3	12	3	Died on 94th day : abscess. One recurrence took place after an interval of 46 days.
	25	100	2	9	0	<i>Living and well 253 days after inoculation.</i>
	26	150	2	9	0	Died on 29th day from pneu- monia.
	27	125	1	3	0	<i>Living and well 226 days after inoculation.</i>
	28	100	1	3	0	Died on 91st day : itch.
	29	100	1	3	0	<i>Living and well 226 days after inoculation.</i>
	30	125	1	4	0	Died on 27th day from pneu- monia.
	31	100	1	4	0	Died on 27th day from pneu- monia.
	32	150	1	4	0	Died on 41st day : itch.

Experiments in which Antimony and Sodium Antimonyl Tartrate were given before Inoculation, in order to Test their Effects upon the Development of the Disease.

In these experiments the substances were given suspended in Colonel Lambkin's medium, and it will be noticed that the metal is far more effective in delaying the appearance of the trypanosomes in the blood than is the salt: this is probably due to the slower elimination of the metal. This method, if the doses were repeated, might be of some practical value in getting animals safely across dangerous tracts of country.

Four Rats were given 5 minims of 5 per cent. Antimony (metal) Cream on December 19. In Nagana the trypanosomes usually appear in the blood on the second or third day after inoculation.

No.	Inoculated with Na-gana on—	Trypanosomes appeared in the blood on—
1	December 20 ...	December 31, the 11th day.
2	" 21 ...	January 2, the 10th day.
3	" 23 ...	December 31, the 8th day.
4	" 24 ...	" 30, the 6th day.

Four Rats were given 3 minims of 5 per cent. Sodium Antimonyl Tartrate Cream on December 19.

No.	Inoculated with Na-gana on—	Trypanosomes appeared in the blood on—
1	December 20 ...	December 25, the 5th day.
2	" 21 ...	" 24, the 3rd day.
3	" 23 ...	" 26, the 3rd day.
4	" 24 ...	" 27, the 3rd day.

Rats treated with Lithium Antimonyl Tartrate.

There are differences in the effects produced by the potassium, sodium, and lithium antimonyl tartrates, if given under similar conditions and dosage. The commercial potassium salt is very impure. The pure sodium and lithium salts which we have used have been prepared for us by Dr. R. H. Aders Plummer, of University College. The sodium salt contains roughly about 2 per cent. more antimony than the potassium salt, and the lithium salt contains about 2 per cent. more antimony than the sodium; but the doses of the lithium salt have to be much smaller than the corresponding doses of the sodium salt. For instance, 0.5 c.c. of a 1 per cent. solution of the lithium salt is fatal to a rat of 125 grammes, and 0.39 c.c. is fatal to a rat of 80 grammes. When the watery solution is injected intramuscularly, it has not caused necrosis of the tissues in rats, but subcutaneously it has

occasionally done so. We have found that the best strength of solution for rats is 0.25 per cent., and of this 0.5 c.c. has been given for a dose.

The following table shows the effects of this dosage:—

—	No.	Total Quantity in c.c. given of 0.25 per cent. solution.	Recur- rences.	Results to August 20.
Na- gana.	1	7	2	Died of disease on 47th day.
	2	7	1	Killed on 47th day, owing to abscess. Emulsion of organs injected into another rat gave negative result.
	3	4.5	1	Allowed to die on 34th day, the date of recurrence.
	4	4.5	0	<i>Alive and well 134 days after inoculation.</i>
	5	4	0	<i>Alive and well 125 days after inoculation.</i>
	6	4	0	<i>Alive and well 134 days after inoculation.</i>
	7	4	0	Died on 42nd day of broncho-pneumonia : no evidence of trypanosomes.
Surra	8	4	0	<i>Alive and well 134 days after inoculation.</i>
	9	5	2	Died of disease on 47th day.
	10	4.5	0	<i>Alive and well 125 days after inoculation.</i>
	11	3.5	2	Died of disease on 18th day : itch.
	12	3	1	Allowed to die : relapse not treated.

From the above it will be seen that five out of these 12 rats are alive and well at periods varying from 125 to 134 days. This salt is much more soluble than either the potassium or sodium compound, which may, perhaps, as well as its greater antimony content, account for its greater effectiveness. It is, however, more irritating subcutaneously in watery solution.

Experiments with Antimony upon Dogs.

In order to see what the effects of antimony would be on the larger and more important animals when suffering from trypanosomiasis, a series of experiments on dogs has been begun. The trypanosome used was that of Surra, which kills dogs of about 20 lbs. in weight in approximately 14 days, as this is the trypanosome which is of practical importance with regard to dogs.

Dr. MacConkey, of the Lister Institute, kindly performed some initial experiments for us. He made some experiments with a 20 per cent. suspension of sodium antimony tartrate in Colonel Lambkin's medium, in order to find the minimum lethal dose, and he found that 0.5 c.c. of this 20 per cent. cream per 10 lbs. of body weight was probably about the full dose. But he also found that, for practical purposes, this 20 per cent. cream was much too strong, as it caused sloughing in every case; indeed, dogs do not seem to bear these suspensions as well as they do solutions. Dr. MacConkey kept one dog alive till the 40th day, and one until the 30th, but both had many relapses.

Profiting by the experience thus gained, we have made further experiments using much smaller doses, with satisfactory results. But we have found, since trying the lithium antimony tartrate

that this acts more effectually and with less irritation than the creams, whether of metal or salt. All the animals tabulated below are in good condition and are gaining in weight.

(Average length of untreated disease, 14 days.)

No.	Weight, in lbs.	Total Quantities given, in Minims.	Recur- rences.	Results to August 20.
1	22	Antimony cream, 5 per cent., 60 m. Sod. ant. tart., 2 per cent., 40 m.	2	No trypanosomes present since July 13; is alive and well on the 62nd day after inoculation.
2	22	Sod. ant. tart., 2 per cent., 80 m. Lith. ant. tart., 2 per cent., 55 m.	2	Had 9 pups during treat- ment; there were 42 days between the two recur- rences; is alive and well on the 62nd day after inoculation.
3	37½	Sod. ant. tart. cream, 5 per cent., 80 m. Sod. ant. tart., 2 per cent., 40 m. Lith. ant. tart., 2 per cent., 90 m.	6	Incorrect dosage seems a probable cause of these relapses; is alive and well on the 62nd day after inoculation.
4	16	Sod. ant. tart. cream, 5 per cent., 40 m. Sod. ant. tart., 2 per cent., 20 m. Lith. ant. tart., 2 per cent., 40 m.	3	Is alive and well on the 53rd day after inocula- tion.
5	13½	Sod. ant. tart. cream, 5 per cent., 35 m. Lith. ant. tart., 2 per cent., 47 m.	3	Is alive and well on the 53rd day after inocula- tion.

The second and third substances mentioned in Column 3 were given at the recurrences. That these dogs are all alive and well encourages us to hope that, as we get a better knowledge of the dosage required, the recurrences may be less frequent.

Experiments made with Rats treated with Antimony, in order to find out in what Organs the Trypanosomes are latent.

The following initial experiments were made in order to find out where the trypanosomes rest during the period in which the peripheral blood is free from them, after treatment with antimony. Further experiments are being carried on for the purpose of ascertaining in what forms they are present in the organs of treated animals.

The rats were inoculated with Nagana, which is less affected by antimony than Surra, and were all treated with four doses of sodium antimony tartrate. The rats were killed at various intervals, and the organs selected (the liver and bone-marrow) were made into an emulsion with a minimum quantity of 0.75 per cent. salt-solution, and injected into other rats in doses of 1 c.c.; the same dose of blood from the heart was also given.

In the following table the signs + and - are used respectively to denote a positive or negative result.

No.	Number of Days after treatment upon which Rats were killed.	Blood.	Liver.	Marrow.
1	7	-	-	-
2	10	-	-	-
3	12	-	-	-
4	14	-	-	-
5	2	-	+	+
6	4	-	+	-
7	3	-	+	+
8	12	-	-	+
9	14	-	-	+
10	16	-	-	+
11	20	-	-	+

From this table it would appear that the bone-marrow is the place where the trypanosomes can live longest, and that the liver is also a place where they can find protection. This is borne out by some experiments we have made upon trypanosomiasis in birds, in which cultivations of trypanosomes can often be made from the bone-marrow when they cannot be made either from the organs or the blood. The doses given to the above rats were rather under those which we should judge to be curative, but in four cases the results were entirely negative.

[*Reprinted from the PROCEEDINGS OF THE ROYAL SOCIETY,*
B. Vol. 81.]

30. A TRYPANOSOME FROM ZANZIBAR.

By Colonel Sir DAVID BRUCE, C.B., M.B., F.R.S., D.Sc., LL.D.,
Army Medical Service, and Captains A. E. HAMERTON,
D.S.O., and H. R. BATEMAN, Royal Army Medical Corps.

(Received September 18th,—Read November 26th, 1908.)

(From the Laboratory of the Royal Army Medical College,
London.)

[PLATES 1 AND 2.]

About the middle of April, 1908, Dr. J. Rose Bradford, F.R.S., had handed over to him by Dr. Edington, F.R.S.E., a rabbit whose blood contained a trypanosome. Dr. Edington stated that he had inoculated the rabbit with blood from a horse he found at Zanzibar suffering from some obscure disease. This rabbit was handed over to one of us (D. B.) by Dr. Bradford for the purpose of keeping the strain alive and, if possible, identifying the species of trypanosoma.

The following notes have since been received from Dr. Edington. The trypanosome was found at Zanzibar, where no trypanosome has formerly been known. It occurred in a horse in a stable among others, of which none were infected. The animal was old, and had been many years in the place. At death the symptoms were like those in surra and nagana, but the spleen was not enlarged, nor was it coloured abnormally. The usual œdema was apparent and most marked in the sheath, up the abdomen, in the chest, and down the posterior limbs.

Dr. Edington inoculated a horse, an ox, and a goat successfully. The disease ran a sub-acute form in the original horse, but in the inoculated one it seemed rather more acute. Inoculated on February 18th, trypanosomes were seen in its blood on the 25th, and by March 1st the sheath was swollen. There was no real fever (102.2° F.) until February 28th, so that in this case the appearance of parasites preceded the fever. On March 7th it had greatly recovered, œdema had subsided, and the weakness of the preceding few days was recovered from. Dr. Edington left on March 8th, and fears the animal was destroyed, as they had no further vote for funds for food, &c.

A young ox, inoculated on February 15th, showed trypanosomes on the 27th. It had fever fairly high, but had recovered before he left, and trypanosomes were exceedingly few. A goat showed high fever, but its blood never showed trypanosomes at any time, although Dr. Edington hunted with very great thoroughness.

Two rabbits were inoculated, one subcutaneously and one intraperitoneally. The former was sent to Dr. Mesnil from Marseilles, but it has shown nothing. It was twice inoculated with big doses, one from a horse and one from an ox. The other Dr. Edington handed over to Dr. Bradford, and from this rabbit the trypanosome under consideration was obtained and studied.

On examining the rabbit's blood, the trypanosome was found to be a small one, with poorly-developed undulating membrane, and no free flagellum. The average length was only 13.5 microns.

Although it is impossible in some cases to name the trypanosomes from their shape and size alone, still it is evident that a trypanosome of this size, with no free flagellum, cannot be *Trypanosoma brucei*, *evansi*, *gambiense*, or several other species which need not be enumerated. The names of such small trypanosomes as *Trypanosoma nanum* (Laveran), *Trypanosoma congolense* (Broden), or *Trypanosoma dimorphon* (Dutton and Todd), at once occur to the mind.

No doubt the tendency in naming these hæmatozoa is to multiply unnecessarily the number of species. But, on the other hand, it is just as great a mistake to lump too many species together, as has been done. If there is some well-marked difference in two trypanosomes, even if alike in shape, such as their power of setting up disease in certain animals, their mode of spreading from the sick to the healthy—it may be in one by tsetse flies, in another by stomoxys, or tabanus, or by other means—then, naturally, it is of great practical use to distinguish them by different specific names.

Again, it might be argued, that if two trypanosomes were different morphologically, but had the same effect on animals, the same distribution and the same carrier, then the two varieties for practical purposes might be included in the same species.

For example, when we have to do with *Trypanosoma gambiense* we at once know that man is susceptible, that the carrier is *Glossina palpalis*, and that we must keep ourselves out of the area of distribution of this fly if we would escape infection. Theories in regard to the spread of sleeping sickness by mosquitoes, stomoxys, fleas, sexual intercourse, and such like, may, for practical purposes, be ignored. If it is *Trypanosoma brucei*, then we know man is not susceptible, but that we must keep our horses, cattle, and dogs out of the area of distribution of *Glossina morsitans*.

The three most important questions to be borne in mind, in classifying trypanosomes, are, what animals are they capable of infecting, the gravity of the infection, and, thirdly, what is the carrier? To these may be added the morphology of the trypanosome, its cultural characteristics, if any, and, if possible, cross-inoculation experiments. If these several facts could be set down for each trypanosome encountered in Africa, then some classification of the African species might be attempted. But it is only for a few species, such as *Trypanosoma gambiense* and *Trypanosoma brucei*, that we have all these data. Take, for example, the case of *Trypanosoma congolense* (Brodén) and *Trypanosoma dimorphon* (Dutton and Todd)—most important trypanosome diseases. Laveran thinks they are distinct on account of a cross-inoculation experiment, but Brodén himself, Rodhain, and Dutton and Todd all seem to lean to their really being one and the same species. With the data at our disposal at present it is impossible to come to a definite decision.

At the present time the classification of the pathogenic trypanosomes is in a state of chaos, and we have no desire to add to the confusion. Nevertheless, we think it will be well to give a description of Dr. Edington's trypanosome, as far as we have been able to study it, in view of the fact that we are starting at once for Uganda to continue the investigation of sleeping sickness.

MORPHOLOGY OF DR. EDINGTON'S TRYPANOSOME.

A. *Living, unstained.*

Dr. Edington's trypanosome in the fresh condition, as seen in a drop of blood from an infected guinea-pig or rat, appears short and stumpy in outline, about twice the diameter of the red blood corpuscles, among which it slowly moves, with, as a rule, its rapidly-vibrating flagellum in front. The posterior or non-flagellar extremity appears blunt and rounded off abruptly, while the anterior tapers off to a fine point. In the fresh preparation the undulating membrane is not much in evidence, though sometimes it can be seen thrown into waves. The contents of the cell are homogeneous, except for a small refractile body at the posterior extremity, which is evidently the micro-nucleus.

B. *Fixed and stained.*

Method of staining.—The method used for fixing and staining the trypanosomes is usually as follows. The blood-film while still moist is exposed to the vapour of a 4-per-cent. solution of osmic acid in distilled water, to which a drop of glacial acetic acid has been added, for 45 seconds. The cover-glass is then transferred to absolute alcohol for from five minutes to half an hour. It is then passed through grades of alcohol from 80 per cent. to 10 per cent. in distilled water. Twenty-five drops of Giemsa's stock stain (Grübler's) are now mixed with 25 c.c. of distilled water. The films are placed in this, face downwards, for 8 to 12 hours, then washed in distilled water, and rinsed quickly in solution of orange tannin (orange G. 1 per cent., tannin 5 per cent., in distilled water). When sufficiently decolorised, the films are washed in distilled water, dehydrated by passing through acetone, cleared in xylol, and mounted in canada balsam.

Dr. Edington's trypanosome when stained in this way appears of a pale puce colour with reddish-purple nucleus and micro-nucleus. The following detailed description must be understood to refer to this trypanosome as found in the blood of the white rat.

Length.—It is no easy matter to measure these small irregularly-shaped bodies, and doubtless the method of measurement used will govern to some extent the result. The method used by us is simply to draw a sharp outline of the trypanosome by means of a Zeiss camera lucida, at a magnification of 2,000 diameters, and then to measure along the middle line of the body by means of a pair of fine compasses, the points of which are separated 2 mm. Each step the compass takes is therefore equal to 1 micron. Twenty trypanosomes, taken as they come, are measured in this way in each specimen, and an average of the 20 measurements taken. The following table gives some of the results:—

Dr. Edington's Trypanosome.

No. of Experiment.	Day of Disease.	Method of Staining.	In Microns.		
			Average Length.	Maximum Length.	Minimum Length.
134, mouse ...	9	Giemsa ...	15·3	20·0	13·0
69, rat ...	30	Leishman ...	13·0	16·0	10·0
" ...	30	Giemsa ...	13·9	17·0	10·0
" ...	30	Methyl green	13·4	18·0	10·0
" ...	30	Giemsa ...	15·0	18·0	13·0
" ...	30	Leishman ...	13·5	17·0	11·0
84, rabbit ...	22	Giemsa ...	13·0	16·0	9·0
Guinea-pig ...	18	" ...	12·5	16·0	8·0
166, dog ...	14	" ...	13·0	16·0	10·0
		Average ...	13·6	17·1	10·4

For purposes of comparison measurements of *Trypanosoma dimorphon* and *Trypanosoma congolense* are given in the following tables:—

No. of Experiment.	Day of Disease.	Method of Staining.	In Microns.		
			Average Length.	Maximum Length.	Minimum Length.
TRYPANOSOMA DIMORPHON.					
Mouse (Laveran and Mesnil).	?	Giemsa ...	13·8	17·0	12·0
116, rat (Breinl) ...	15	„ ...	13·8	16·0	11·0
„ „ ...	9	Leishman ...	11·3	14·0	9·0
„ „ ...	9	„ ...	12·6	15·0	11·0
Dog (Harvey, Sierra Leone).	?	„ ...	12·3	15·0	9·0
Cow (Smith, Sierra Leone).	?	„ ...	12·4	15·0	10·0
		Average ...	12·5	15·3	10·3
TRYPANOSOMA CONGOLENSE.					
142, mouse ...	7	Giemsa ...	12·8	15·0	10·0
143, mouse ...	5	Leishman ...	11·5	14·0	10·0
152, rat ...	11	Giemsa ...	11·6	15·0	9·0
„ „ ...	11	„ ...	11·5	14·0	10·0
154, rat ...	19	„ ...	12·6	17·0	10·0
		Average ...	12·0	15·0	9·8

Breadth.—On an average the breadth at the widest part is 3 microns.

Shape.—Dr. Edington's trypanosome when stained is seen to be of a short and stumpy shape, somewhat reminding one of a miniature electric eel. The posterior extremity is, as a rule, blunt, or rounded or obtuse-angled, but sometimes, though rarely, it is prolonged into a sharp beak-like process. The anterior end tapers more or less, and ends in a short stout flagellum. The undulating membrane is narrow but distinct. The flagellum arises at or near the micro-nucleus and passes along the edge of the undulating membrane. There is no free flagellum, the protoplasm of the cell and the undulating membrane extending as far as the tip of the flagellum.

Contents of Cell.—The protoplasm, which is stained a pale puce colour, is homogeneous in structure.

Nucleus.—The nucleus is oval in shape, about 2·5 microns in length, and is situated at the centre of the trypanosome.

Micro-nucleus.—The micro-nucleus, centrosome, or kinetocore, is small, round, or rod-shaped, and is situated close to the posterior extremity. It stains more deeply than the nucleus.

Undulating Membrane.—The undulating membrane is narrow. As a rule it is straight and simple, and does not show much tendency to be thrown into folds.

Flagellum.—The flagellum stains intensely. It is well marked, and does not project beyond the protoplasm of the cell and the undulating membrane. Sometimes, in faintly-stained

specimens, there is the appearance of a slight projection of the flagellum beyond the body; but, speaking broadly, this species of trypanosome may be said to have no free flagellum.

The conclusion to be drawn from a study of the morphology of Dr. Edington's trypanosome, *Trypanosoma dimorphon*, and *Trypanosoma congolense*, is, that the two first resemble each other very closely, whereas *Trypanosoma congolense* seems to be of a somewhat shorter and stouter form. It will also be seen that in the strain of *Trypanosoma dimorphon* used there is only one form, and that, the short or tadpole form described by Dutton and Todd. With regard to this, it may be of interest to quote some remarks of Dr. Breinl, to whom I am obliged for his courtesy in sending me this strain. He writes:—"With regard to *Trypanosoma dimorphon*, you are aware that some remarkable change has occurred in the strain between the time Drs. Dutton and Todd brought it back from Africa and we started work on it here. Whereas Drs. Dutton and Todd describe the long flagellated forms with the free flagella, Thomas and myself, Laveran and Mesnil, could not see these forms with a thin body and a long flagellum. The strain I send you in a rat is the original strain."

It is difficult to understand how this change in morphology has been brought about. It may be that Dutton and Todd were dealing with a double infection, of which one has died out. This point will require to be investigated on the spot.

Another matter for consideration is whether this name *Trypanosoma dimorphon* should be adhered to. It certainly seems a misnomer when applied to the strain figured above. If it should be decided to drop it, I think the compliment should be paid to Dr. Todd of naming it after him.

Inoculation Experiments on various Species of Animals.

The animals, in which the effect of the inoculation of Dr. Edington's trypanosome has been studied, have been horses, cattle, goats, monkeys, dogs, rabbits, guinea-pigs, white rats, and mice. The inoculations were made, as a rule, intraperitoneally. Inoculation experiments with *Trypanosoma dimorphon* are also given for purposes of comparison. These are printed in italics:—

No. of Experiment.	Source of Virus.	Period of Incubation, in Days.	Duration of Disease, in Days.	Remarks.
HORSES.				
Edington	Unknown	Unknown	Unknown	Dr. E. thinks ran sub-acute course.
"	Horse	7	"	Living after 18 days when Dr. E. left.
<i>Dutton and Todd ...</i>	<i>Natural infection.</i>	<i>Unknown</i>	<i>25 years, still alive.</i>	<i>Blood still infective.</i>
"	"	"	<i>1 year, still alive.</i>	<i>No record.</i>
<i>Laveran</i>	—	"	—	<i>Horse recovered.</i>

No. of Experiment.	Source of Virus.	Period of Incubation, in Days.	Duration of Disease, in Days.	Remarks.
--------------------	------------------	--------------------------------	-------------------------------	----------

CATTLE.

Edington	Horse	12	Unknown	Animal looked well on 21st day.
Dutton and Todd...	—	10.5	30	Two cattle.

GOATS.

Edington	Horse	Unknown	Unknown	Blood never showed trypanosomes up to 18th day.
Dutton and Todd...	—	3.5	Well after a year.	Two goats.

MONKEYS.

174	Rat	3	22	Spleen enlarged. General glandular enlargement.
175	"	3	—	Still alive (Sept. 11, 1908).
Thomas and Breinl	—	4 and 6	160 and 75	Two monkeys.
Dutton and Todd...	—	4	—	Two never became infected.

DOGS.

165	Rat	7	18	Spleen enormously enlarged.
166	"	9	15	" "
167	"	7	17	" "
179	"	7	14	Marked ulceration of stomach.
180	"	9	14	Spleen greatly enlarged.
181	"	7	14	" "
Thomas and Breinl	—	4 to 8	10 to 19	Average of 4 days.
Dutton and Todd...	—	8	29	

RABBITS.

70	Rabbit	25	—	Still alive after 146 days.
84	"	10	—	Still alive after 136 days.
118	"	12	100	Spleen 4 inches long and much thickened.
119	"	15	—	Still alive after 103 days.
120	"	12	19	Spleen enlarged.
Thomas and Breinl	—	9	Acute, 26—35; chronic, 78—157.	One rabbit.
Dutton and Todd...	—	13	53	

No. of Experiment.	Source of Virus.	Period of Incubation, in Days.	Duration of Disease, in Days.	Remarks.
GUINEA-PIGS.				
82	Rabbit	25	134	Liver and spleen enlarged.
110	Rat	12	43	Liver and spleen greatly enlarged.
111	"	19	43	Still "alive after 105 days.
124	"	21	—	
125	"	21	69	Liver and spleen enlarged.
126	"	41	65	<i>Two "guinea-pigs."</i>
<i>Dutton and Todd...</i>	—	6	30	
<i>Thomas and Breinl</i>	—	4 to 15	9 to 60	
WHITE RATS.				
69	Rabbit	13	30	Typical <i>post-mortem</i> appearances.
83	"	10	—	Killed for cultivation experiments.
83A	"	11	—	Usual " <i>post-mortem</i> appearances.
127	"	7	41	
128	"	7	36	2nd "passage" through rat.
88	Rat ii	5	20	
89	" ii	5	—	Killed for cultivation experiments.
106	" ii	5	—	Typical " <i>post-mortem</i> appearances.
107	" ii	4	14	
108	" ii	7	35	" "
109	" ii	5	28	
102	" iii	6	—	Killed "for cultivation experiments.
102A	" iii	7	37	Usual <i>post-mortem</i> appearances.
121	" iii	4	37	" "
122	" iii	5	44	
123	" iii	4	—	Rat lost.
156	" iii	7	20	Usual <i>post-mortem</i> appearances.
157	" iii	7	23	" "
<i>Dutton and Todd...</i>	—	7	36	
<i>Thomas and Breinl</i>	—	4 to 7	7 to 42	
MICE.				
132	Rat	10	24	
134	"	4	11	
137	"	10	11	
<i>Dutton and Todd...</i>	—	5	16	
<i>Thomas and Breinl</i>	—	2 to 5	16 to 23 37 to 130	

Conclusion.—The results of these inoculation experiments with Dr. Edington's trypanosome and *Trypanosoma dimorphon* show that they act on the various animals employed in a strikingly similar manner.

CULTIVATION OF DR. EDINGTON'S TRYPANOSOME, *Trypanosoma dimorphon* AND *Trypanosoma congolense*.

In June, 1903, Novy and MacNeal first announced the successful cultivation of *Trypanosoma lewisi*. In the same year and in the following year they also succeeded in cultivating *Trypanosoma brucei* and *Trypanosoma evansi*. These gentlemen deserve the highest possible credit for this most difficult achievement, an achievement which most workers in this subject thought impossible. The amount of work they expended and the splendid intelligence and pertinacity with which they pursued their object, refusing to accept defeat, command the admiration of all their co-workers in this branch of biological science. Since then the trypanosomes of birds, frogs, and fish have been cultivated by the same and other workers; but these successes have only been made possible, as a rule, by the pioneer work of Novy and his assistants. Coming out of their work, mention may also be made of the very interesting and important observation made by Rogers when he grew Leishman's bodies in ordinary citrated blood into trypanosome-like flagellates.

One of the chief interests attaching to this cultivation of trypanosomes is that it may assist in separating the different species of these organisms. At the present time trypanology is in a state of chaos on account of this difficulty in differentiation. Many diseases of animals caused by trypanosomes have been reported from all parts of Africa, Arabia, India, the Philippines, Mauritius, &c., and it has often been found impossible to name the species of trypanosoma causing them with any approach to certainty.

As mentioned above, the usual method of separating the different species is by taking into consideration the morphology, the result of inoculation into animals, the cross-immunisation methods and serum diagnosis of Laveran and Mesnil, the mode by which the disease spreads from the sick to the healthy—by a tsetse fly, a stomoxys, a tabanus, or by contact, as in dourine—by the effect of various drugs, cultivation, &c.; and, as already stated, the effect the parasite has on animals and the mode of conveyance are probably, for practical purposes, the most important. But to assist in separating the various species, cultivation has been of use in the past, and, as the methods become perfected, will be of still greater use in the future.

The following description of the cultural characters of Dr. Edington's trypanosome exemplifies this, for, by comparing them with the cultural characters of other pathogenic species, a fairly shrewd guess at its classification may be made by this means alone. For the purpose of this comparison a compilation of the cultural characters of *Trypanosoma lewisi*, *Trypanosoma brucei*, and *Trypanosoma evansi* has been made from the writings of Novy, MacNeal, and Smedley.

It may be mentioned here that attempts have been made in this laboratory to cultivate these three species. The cultivation of the first was found to be a comparatively easy matter; but all attempts, and they were many, to cultivate the last two have, up to the present, failed, although Novy's instructions were carefully followed.

Cultivation Medium used.

The blood-agar medium used was made according to instructions kindly sent by Professor Novy. These need not be repeated here, as the details are fully given by Novy and MacNeal in various papers.

CULTURAL CHARACTERS OF *Trypanosoma lewisi*.A. *Living, unstained.*

Size.—Varies considerably in size. Some are not more than 1 or 2 microns long, not including the flagellum. Others are about the diameter of a red blood corpuscle, while the usual length of the spindle-shaped cells is 15 to 20 microns. Some trypanosomes can be found at times which are 50 to 60 microns long. The greatest variation in size is found in young cultures.

Shape.—*Trypanosoma lewisi* varies greatly in shape, as well as in size. Round, pear-shaped, fusiform and slender forms are present in the cultures. The round forms are usually found in old cultures, and are probably involution forms.

Contents of Cell.—The protoplasm in *Trypanosoma lewisi*, especially in young cultures, is bright, glistening, and apparently homogeneous in structure in the fusiform and slender forms.

Undulating Membrane.—Not present as far as can be seen. The movement of these cultural forms appears to be entirely due to the rapid motion of the flagellum.

Flagellum.—These forms possess, as a rule, a long free flagellum. In the slender forms this is sometimes twice the length of the body.

Motion.—The single, slender, cultural forms of *Trypanosoma lewisi* are very active, and dart across the field of the microscope in a straight line. In older cultures the round and other involution forms do not, as a rule, show more than a slight swaying movement.

Colonies or Aggregations.—Growth commences in a first generation about the fifth day by the appearance of small rosettes composed of a few trypanosomes. The Colonies rapidly grow, so that on the following day masses of wriggling trypanosomes may be seen. These aggregations of twenty or more are attached by their flagella. They grow larger and larger until, about the twenty-fourth day, they are apparent to the naked eye, and consist of many thousands of trypanosomes.

B. *Fixed, stained.*

Protoplasm.—Homogeneous, as a rule. Vacuolation is rare, but sometimes a large highly-refractile vacuole is seen.

Nucleus.—Round or oval in shape. Situated centrally or at the junction of the anterior and middle thirds.

Micro-nucleus.—Is placed either close to the nucleus or at a variable distance anterior to it. In the free forms it is never seen lying posterior to the nucleus. As a rule, it is a rod-shaped structure, lying transversely to the long axis of the trypanosome.

Flagellum.—Arises from the vicinity of the micro-nucleus. The free flagellum is often two, three or four times the length of the body of the trypanosome.

Undulating Membrane.—In the cultural form of *Trypanosoma lewisi* this structure is apparently absent.

Colonies or Aggregations.—There is little to add to the description of the trypanosomes and of their arrangement in Colonies. Stained preparations show that the trypanosomes sometimes possess very long flagella. Novy and MacNeal* have not apparently succeeded in staining the flagellum in their preparations, though they noted the position of the centrosome. They expressed the opinion that the end of the trypanosome pointing towards the periphery of the Colony was the anterior extremity, and that from it a flagellum would arise if the cultural conditions were perfected (Smedley).

Measurements of the Cultural Forms of Trypanosoma lewisi.

Pear-shaped Forms.—(1) Body, 3.6 to 4.4 microns long, and nearly as broad. (2) Flagellum, two to four times the length of the body.

Spindle-shaped Forms.—14 to 16 × 2.4 to 3.5 microns, flagellum not included.

Smaller and larger forms are frequently found.

The adult parasitic form of *Trypanosoma lewisi* measures 24 to 25 × 1.5 microns (Laveran and Mesnil) (Smedley).

CULTURAL CHARACTERS OF *Trypanosoma brucei*.

A. *Living, unstained.*

Size.—Shows less variation in size than *Trypanosoma lewisi*, and averages 15 microns in the living condition. Smaller than those found in the blood.

Shape.—Do not vary much in shape, and closely resemble the forms found in the blood (Smedley).

Contents of Cell.—Show one or two very large, bright, and highly-refracting globules, usually placed near the anterior or flagellar end, in the otherwise homogeneous colourless cell. In size the globules may attain 1 micron. At times the number of these globules is increased, as when the culture is kept at 34° C. The presence of numerous large, highly-refractile globules in the cultural forms of *Trypanosoma brucei* is attributed by Novy and MacNeal to degeneration of the organisms, owing to imperfection of the culture medium. These globules become more numerous as the age of the culture advances. Do not seem to alter in position or shape if kept under observation for several hours. Resist staining completely. Laveran and Mesnil suggest that the globules are of the same nature as the refringent, unstainable granules found in *Trypanosoma rotatorium*.

Undulating Membrane.—No detailed description available.

* 'Cultivation of *Trypanosoma brucei*,' p. 28.

Flagellum.—The flagellum in the living cell is by no means as distinct and as long as that of *Trypanosoma lewisi*.

Motion.—The motion of *Trypanosoma brucei* is slow and wriggling, and only exceptionally is a slowly-progressive form observed. The wave-motion slowly passes along the thick, undulating membrane, and gives the appearance of a spiral rotation to the entire cell. Scarcely departs from its place (Novy). In a young culture the trypanosomes are found to possess very active movements. Sometimes they advance across the field moderately quickly, but their rate of movement is always much slower than that of the rat trypanosomes, whose flagella are longer and more rapid in motion (Smedley).

Colonies or Aggregates.—Occurs in groups or rosettes. Rarely forms masses of more than 10 to 20 cells. The individuals are long, narrow, and show the peculiar writhing motion. The flagella are directed outwards, and the appearance of the whole may be compared to the snakes on a Medusa head. The stellate group with the bright, refracting globules within the cells, suggests a jeweller's "sun burst" (Novy). The active movements of the trypanosomes, and the large glistening vacuoles with which they are studded, give these colonies a singularly beautiful appearance (Smedley).

B. *Fixed, stained.*

Protoplasm.—The protoplasm invariably contains a few deeply-stained granules of a red or violet colour. The vacuoles are seen as clear circular spaces with sharply-defined outlines in stained preparations (Smedley).

Nucleus.—Round or oval in shape; and in older forms it breaks into masses of cromatin, which are found distributed through the protoplasm of the cell (Smedley).

Micro-nucleus.—This is much smaller than in *Trypanosoma lewisi*; it is usually circular, but sometimes elongated. It stains a deep red or purple colour, and it is sometimes difficult to distinguish it from the other granules. It is generally found close to the vacuole; sometimes it lies close to the nucleus, but it is nearly always posterior to the latter structure (Smedley).

Flagellum.—Takes a tortuous course along the free border of the undulating membrane, and projects for a short distance from the anterior extremity (Smedley).

Undulating Membrane.—No detailed description given.

Colonies or Aggregates.—Most of the flagella are directed in an outward direction. It is rare to find Colonies of a large size (Smedley).

Measurements of the Cultural Forms of Trypanosoma brucei.

Length, including flagellum, 18 to 23 \times 2.5 to 3.5 microns. Length of free flagellum, 3 to 5 microns. Diameter of vacuoles, 1 to 2 microns. The adult parasitic forms of *Trypanosoma brucei* measure, in the blood of rats, 26 to 27 \times 1.5 to 2.5 microns (Laveran and Mesnil) (Smedley).

CULTURAL CHARACTERS OF *Trypanosoma evansi*.A. *Living, unstained.*

Size.—The body of one large individual measured 21 microns, while the flagellum was 28 microns in length.

Shape.—The slender fusiform body terminates at one end in a delicate flagellum. The posterior end, especially when blunt, showed a rod-like tip or stylet, which varied from 2 to 4 or even 6 microns in length. As the cultures aged, pear-shaped or spherical, highly granular, involution forms appeared. In the former type, measuring about 3 by 5 microns, the end was often provided with a flagellum, 10 to 15 microns long, which still showed a slow lashing movement, though the cell itself was motionless. The spherical forms varied from 4 to 9 microns in diameter, were granular, and often showed a remnant of the flagellum as a short, stiff, motionless whip. These involution forms, as in the case of *Trypanosoma lewisi* and *Trypanosoma brucei*, eventually gathered into large groups or masses, which at times filled the field of an immersion lens. Later on, the round bodies broke up into masses of very minute granules.

Contents of Cell.—Presence and peculiar arrangement of granules within the cells, and a distinct yellowish or greenish colour of the granules and of the contents. Large numbers of small granules or globules, which vary from 0.3 to 0.5 micron in diameter. These globules, as well as the contents of the cell, possess a decided yellowish or greenish colour, and appearance quite unlike that of either *Trypanosoma lewisi* or *Trypanosoma brucei*. The globules are usually massed in the anterior-third of the cells—that is, at the base of the flagellum, and only a few isolated granules are scattered through the remainder of the organism (Novy and MacNeal).

Undulating Membrane.—Is not recognisable in the living organism.

Flagellum.—Usually as long and often even longer than the cell itself.

Motion.—All single and actively motile, traversing the field of the microscope at great speed. Travel with the flagellum in rear or in front.

Colonies or Aggregates.—Entire absence of the groups or rosettes, which are so characteristic of the cultures of *Trypanosoma lewisi* and *Trypanosoma brucei*. The trypanosomes were all single and actively motile.

Measurement of the Cultural Forms.

Length, including flagellum, 25 to 50 by 1.5 to 2.5 microns.

CULTURAL CHARACTERS OF DR. EDINGTON'S TRYPANOSOME.

A. *Living, unstained.*

No difficulty is found in cultivating Dr. Edington's trypanosome. As early as the second day, if kept at 25° C., it is found to have greatly increased in numbers. The single individuals are

in active motion, the flagellum wildly waving, while the body slowly moves among the corpuscles. Many dividing forms are seen with two or three flagella. Masses or aggregations are also seen varying in size, from those composed of a dozen individuals to those occupying a fifth of the field. The aggregation-forms are all writhing and squirming, while the flagella at the periphery are frantically waving. This incessantly moving mass, dotted over as it is with many small bright vacuoles, makes a curious and beautiful microscopic object when brightly illuminated.

On the third day the trypanosomes have multiplied to an extraordinary extent. Huge aggregations are now seen, each filling up several fields of the microscope. The individual trypanosomes are still actively motile. Single, double, and small aggregations are also seen.

By the seventh day they have reached the height of their growth and begin to degenerate.

After the twelfth day living forms can no longer be recognised in the culture tubes.

Size.—Dr. Edington's trypanosome, examined in the fresh living condition, varies considerably in size. Some of the large forms measure 32 microns in length, whereas the smaller are only half that length, or even shorter.

Shape.—So also in regard to shape, these cultural forms vary extremely. Round, oval, pear-shaped, and irregular forms are seen. Slender forms shaped like ordinary trypanosomes, with a beak or rostellum at one end, a fairly thick flagellum at the other, and furnished with an undulating membrane, are fairly common. Large irregular masses of any shape, furnished with one or more flagella, are also frequent.

Contents of Cell.—These cells have a remarkable appearance, as they are filled with highly refractile granules, large in size, round in shape, and numerous.

Undulating Membrane.—The round, oval, and pear-shaped forms do not appear to possess an undulating membrane, whereas the long, slender forms, as also the huge fish-shaped or octopus-like forms, often show well-marked undulating membranes.

Flagellum.—The flagella in these living unstained cultural forms are thick and coarse, and differ markedly from the slender structures usually associated in the mind with trypanosomes. Just as in the parasitic forms found in the blood, it is evident that the protoplasm of the body extends to the tip of the flagellum giving rise to this thick stumpy appearance.

Motion.—The slender forms are active and swim fairly quickly across the field. The large, irregular forms are stationary, but exhibit actively wriggling flagella and amœboid movements of the body substance.

Colonies or Aggregates.—Colonies or aggregations of 10 to 20 individual cells are common. The cells are arranged irregularly. Some of their flagella may be directed outwards, while others are seen entangled in the mass and feebly wriggling. On the third day these aggregations may be seen as large as three to five fields of the microscope, and must be composed of many thousands of individual trypanosomes.

B. Fixed, stained.

Method of Fixing and Staining.—The cultural forms of Dr. Edington's trypanosome were either prepared by mixing a drop of the cultivation fluid with fresh serum, spreading on a slide, and staining by Leishman's modification of Romanowsky's method, or the fluid was spread on a slide, fixed by osmic acid and stained by Giemsa, and then treated with orange tannin to differentiate the various structures.

In Leishman-stained preparations the protoplasm of the cells is stained a pale blue, the nuclei and irregular masses of chromatin reddish or pink, while the vacuoles stand out as unstained spaces with sharply-defined margins. In Giemsa-stained preparations, on the other hand, the protoplasm is stained a pale puce colour, while the chromatin material is stained reddish purple.

Protoplasm.—The protoplasm of the cell is homogeneous, but contains irregular-shaped granules and masses of chromatin-staining material. There are also present numerous well-marked vacuoles of various sizes, which are unstained, and, as mentioned above, highly refractile.

Nucleus.—The nuclei are of every form and shape, and often broken up into irregular masses.

Micro-nucleus.—The micro-nuclei are irregularly placed; in some cells are not easily distinguishable from other granules contained in the protoplasm, but in many are clearly seen as deeply-staining bodies, round or rod-shaped, in close connection with the point of origin of the flagella.

Flagellum.—The flagella are, as a rule, thick and fleshy. In the irregular forms they appear to spring from any part of the shapeless mass of protoplasm, and in any direction.

Undulating Membrane.—The undulating membrane is also characterised by its extreme irregularity. In many cells it appears to be absent, while in others it is well marked, broad, and thrown into folds.

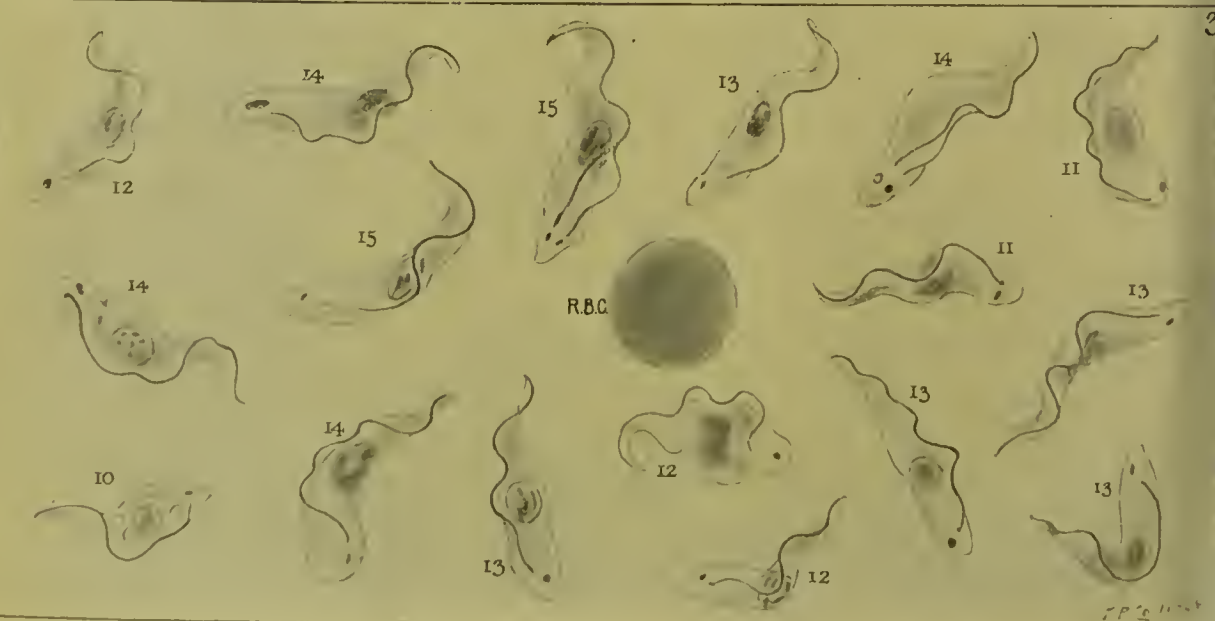
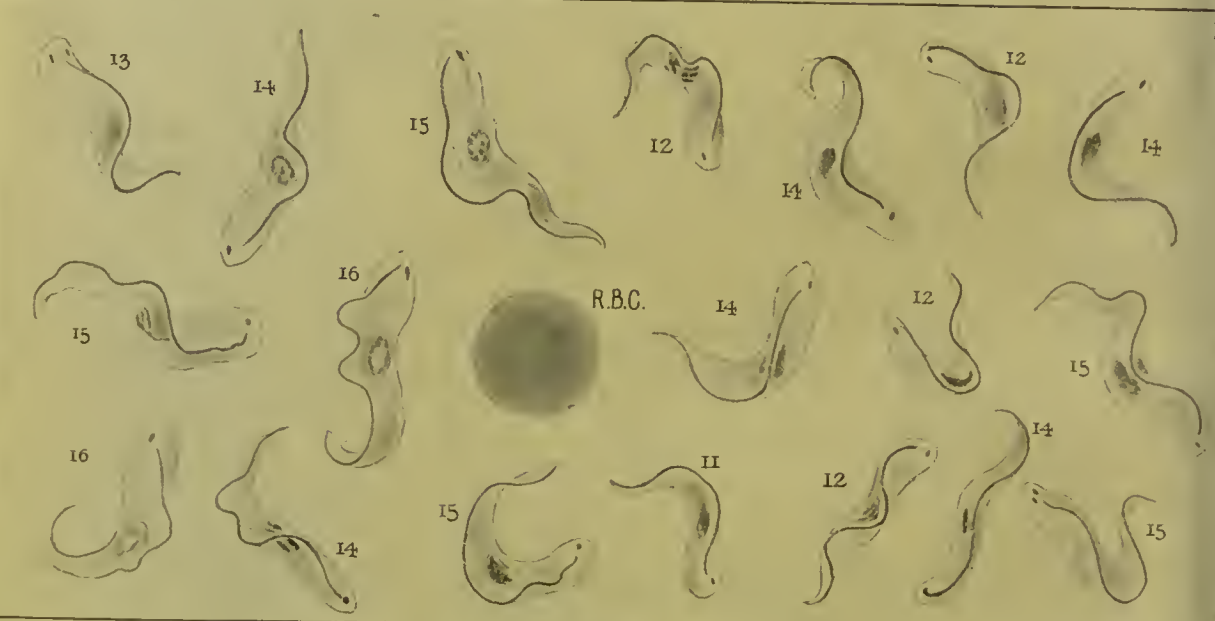
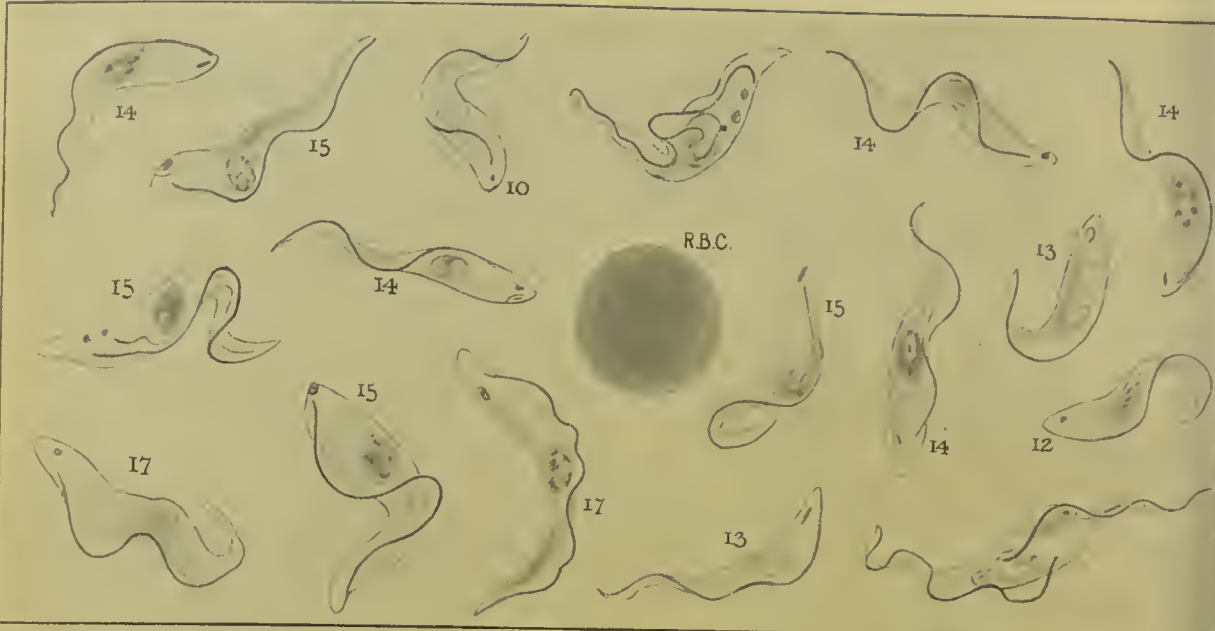
Colonies or Aggregations.—The individual trypanosomes which go to compose the large aggregations are as a rule short and stumpy in form, with oval-shaped nucleus and short stumpy flagellum. They are of irregular shape and size, and are placed without any seeming order.

CULTURAL CHARACTERS OF *Trypanosoma dimorphon* (DUTTON AND TODD).

It is unnecessary to describe in detail the cultural characters of this trypanosome, as they agree exactly with those of Dr. Edington's.

CULTURAL CHARACTERS OF *Trypanosoma congolense* (BRODEN).

Several attempts were made to cultivate *Trypanosoma congolense*, but none of them were very successful. There is certainly not the rapid growth of this trypanosome which distinguishes Dr. Edington's trypanosome and *Trypanosoma dimorphon*. It is only after a long search that individual trypanosomes can be found in the preparations. There is no formation of masses or





aggregations filling several fields of the microscope as in the others. It is difficult to say whether there is any real multiplication or not. All that can be said is that, for about eight days, living trypanosomes can be seen. At first these are shaped like the ordinary trypanosomes found in the blood, only larger and swollen in appearance; but by the fifth and following days these change into most irregular and fantastic shapes. Nothing living could be seen after the eighth day. This cultivation experiment would therefore seem to strengthen Dr. Laveran's opinion that *Trypanosoma dimorphon* and *Trypanosoma congolense* are distinct species.

Conclusion.

The conclusion arrived at is that Dr. Edington's trypanosome from Zanzibar is probably Dutton and Todd's *Trypanosoma dimorphon*. One link in the chain of evidence, however, is wanting, and that an important one—the identity or non-identity of the carrier.

DESCRIPTION OF PLATES.

PLATE 1.

This plate represents the shape and size of the three Trypanosomes, viz. :—

1. Dr. Edington's trypanosome. From blood of rat. 30th day of disease. Stained Giemsa. $\times 2000$. See p. 26.
2. *Trypanosoma dimorphon*. From blood of rat. 15th day of disease. Stained Giemsa. $\times 2000$. See p. 26.
3. *Trypanosoma congolense*. From blood of mouse. 7th day of disease. Stained Giemsa. $\times 2000$. See p. 26.

PLATE 2.

FIG. 1.—Part of an aggregation of Dr. Edington's trypanosomes after 5 days' growth. Stained Giemsa. $\times 2000$.

FIGS. 2-4.—Dr. Edington's trypanosome after 6 days' growth. Stained Giemsa. $\times 2000$.

FIGS. 5-14.—Cultural forms of Dr. Edington's trypanosome after 7 days' growth. Stained Leishman. $\times 2000$.

[Reprinted from the PROCEEDINGS OF THE ROYAL SOCIETY,
B. Vol. 81.]

31. TRYPANOSOMA INGENS, n. sp.

By Colonel Sir DAVID BRUCE, C.B., F.R.S., Army Medical Service; Captains A. E. HAMERTON, D.S.O., and H. R. BATEMAN, Royal Army Medical Corps; and Captain F. P. MACKIE, Indian Medical Service.

(Received April 30,—Read May 20, 1909.)

(Sleeping Sickness Commission of the Royal Society, 1908—09.)

[PLATE 3.]

This is such an extraordinary looking parasite that the Commission thinks it deserves a short preliminary note, a name, and to be figured.

The name is taken from Virgil's description of the Cyclops, *informe, ingens*. It was first discovered in the blood of a reed-buck on February 13, 1909, at Namukekera, Uganda (lat. $0^{\circ} 40'$ N.; long. $32^{\circ} 15'$ E.), the estate of the Uganda Company, Limited; then in a bush-buck, and lastly in an ox. The wild animals and the cattle feed in the same pastures, so that it is not remarkable that the oxen should become infected.

At present it is not known what the carrier is, and this will probably be a difficult thing to determine. Collections of the blood-sucking flies and ticks are being made on the Namukekera Estate, and this may lead in time to the discovery of the carrier. Up to the present the following list includes all the blood-suckers found in this particular district:—

Chrysops distinctipennis, Austen.

Stomoxys calcitrans, Linn.

Stomoxys nigra, Macq.

Tabanus taniola, Pal de Beauv.

Hæmatopota unicolor, Ricardo.

Hæmatopota, sp. nov.

Hæmatopota brunnescens, Ricardo.

Trypanosoma ingens, when seen alive in a fresh preparation, moves slowly and deliberately across the field of the microscope, with a fine rippling, or at times a broader undulating movement.

In stained preparations this huge trypanosome may measure as much as 122 microns, and even then it is lying in such a formless huddled-up way among the red blood corpuscles that it looks capable of stretching out to a much greater length. The other specimens figured measure 72, 77, 88, and 82 microns. The breadth is 7 to 10 microns.

The micronucleus is small and round. It measures about a micron in diameter. It lies posterior to, and quite close to, the nucleus. From it, in well-stained specimens, a well-marked, though narrow, undulating membrane arises, which runs to the anterior extremity and ends in a free flagellum.

The nucleus is oval in form, and lies across the body. It is situated nearer the posterior end than the anterior, and in our specimens has stained a pale pink.

The body substance is markedly granular behind the nucleus, while in front the structure described as myonemes is particularly well marked.

More minute measurements of one of these trypanosomes are as follows:—

Posterior end to micronucleus...	18
From micronucleus to nucleus	4
Nucleus: long diameter, 8 microns; short diameter				4
Nucleus to anterior end	40
Free flagellum	17
				—
Total	83

It is unnecessary in this preliminary note to go more fully into the structure of this trypanosome, or to describe it at greater



length. An examination of the coloured drawings reproduced in Plate 3 will give a more distinct idea of its appearance than any written description.

The drawings were made by Lady Bruce, R.R.C. Figs. 1, 3, and 4 are from reed-buck, fig. 2 from the ox. All are magnified 2,000 and stained Giema.

[*Reprinted from the* PROCEEDINGS OF THE ROYAL SOCIETY,
B. Vol. 81.]

32. FURTHER RESULTS OF THE EXPERIMENTAL TREATMENT OF TRYPANOSOMIASIS: BEING A PROGRESS REPORT TO A COMMITTEE OF THE ROYAL SOCIETY.

By H. G. PLIMMER, F.L.S., and W. B. FRY, Captain R.A.M.C.

(Communicated by J. Rose Bradford, M.D., Sec. R.S.
Received June 28, 1909.)

The following results are a continuation of the work of which summaries have already appeared in the "Proceedings of the Royal Society."*

These experiments have been carried out, with the same strain of Surra as was used before, at the Brown Institution and the Lister Institute.

A.—*Condition of the Animals living at the Date of the Completion of the Tables in the last Paper.*

Rats treated with Sodium Antimonyl Tartrate, 1 per cent. (p. 478).

No. 7	died	428	days	after	inoculation.
„ 32	„	409	„	„	„
„ 35	„	371	„	„	„

*Rats treated with Sodium Antimonyl Tartrate, 5 per cent., in
Colonel Lambkin's Medium (p. 482).*

No. 13 died 216 days after inoculation.

*Rats treated with Antimony (metal), 5 per cent., in Colonel
Lambkin's Medium (p. 483).*

No. 10	died	205	days	after	inoculation.
„ 17	„	367	„	„	„
„ 25	„	385	„	„	„
„ 27	„	399	„	„	„
„ 29	„	360	„	„	„

* B, vol. 79, 1907, pp. 500–516 ; and B, vol. 80, 1908, pp. 1–12 and 477–487,

Rats treated with Lithium Antimonyl Tartrate, 0.25 per cent.
(p. 485).

No.	4	died	145	days	after	inoculation.
„	5	„	229		„	
„	6	„	257		„	
„	8	„	241		„	
„	10	„	209		„	

Most of the above rats died from cold; none of them died from the disease, and no trypanosomes were found in their blood or organs, and inoculations made therefrom were entirely negative.

B.—*Further Experiments.*

Rats treated with Lithium Antimonyl Tartrate, 1 per cent.

A further series of experiments has been carried out with this substance on a large number of rats, giving four doses of 4 to 5 minims (according to weight) of a 1 per cent. solution subcutaneously, a dose being given every other day. Practically by this method every rat can be cured. They have lived for varying periods, up to 249 days, and in no case have trypanosomes been found after death in the blood or in the organs. No rat has died of the disease, and in no case thus treated has there been a recurrence. The results have therefore been more constant than those attained with sodium or potassium antimonyl tartrates. The treatment was begun on the third or fourth day after inoculation; it will be seen below that when it is left until the number of trypanosomes in the peripheral blood is very great, although they may be driven out of the blood, it does not cure: so that the time at which treatment is commenced is of considerable importance.

It has also been given intravenously in rabbits, but with far less effect than when given subcutaneously. The elimination in this case is very rapid, to which fact we attribute its comparatively feeble action.

Rats treated with Lithium Antimonyl Tartrate on the Fifth or Sixth Day of the Disease.

The blood at this period of the disease is swarming with trypanosomes, and experiments were made in order to see what effect this salt of antimony would have upon the disease at this period. If one dose of 5 minims of a 1 per cent. solution be given the rats die on the seventh day, so that little or no effect is produced. If two such doses be given, one on the fifth and one on the sixth day, the average time of death in 10 rats was $19\frac{1}{2}$ days, and living trypanosomes were found in the blood at death. When four doses were given, one on each day from the fifth to the eighth, the time in three rats was lengthened to 81 to 86 days: in one of these even living trypanosomes were found in the blood after death. By comparing these results with those mentioned in the former section

it will be seen that the time at which the administration of the drug is begun is of importance, as well as the number of doses. The animals stand the best chance of cure when no recurrences take place, and this is best ensured by the method described in the previous section.

Further experiments made with Rats treated with Antimony in order to find out in what Organs the Trypanosomes are latent.

Following on the experiments made on rats treated with sodium antimonyl tartrate, with the view of finding out where the trypanosomes are latent, and recorded in the last paper,* a further series of experiments has been made on rats inoculated with Surra, which is more amenable to treatment with antimony than the Nagana used in the former series, and completely treated (that is, given a curative series of doses) with lithium antimonyl tartrate: this, as stated in the paper referred to, appears to be the most active of this variety of salt.

Seven rats were treated with four doses of 5 minims of a 1 per cent. solution of lithium antimonyl tartrate, and they were killed in succession, one on the 6th, 7th, 10th, 14th, 16th, 22nd, and 30th days after the last dose. The livers and bone-marrow were made into an emulsion with the minimum quantity of 0.89 per cent. salt solution, and 1 c.c. of the emulsions of these organs and 1 c.c. of heart's blood was injected separately into other rats. The results were entirely negative. Microscopic preparations were made of the material injected and no organisms were seen, and none of the sub-inoculations gave a positive result.

Experiments made in order to see if any Protection was afforded by Initial Treatment with Antimony.

A series of six rats was treated with four doses of 5 minims of a 1 per cent. solution of lithium antimonyl tartrate, one dose every other day in the same manner as when given for curative purposes. They were then inoculated with Surra, one on the first day after the completion of the treatment, and one on the 2nd, 4th, 5th, 9th, and 10th days after. They all died on the 5th or 6th days after inoculation, just as untreated rats would have done, so that antimony in this very soluble form is of no protective use in rats, owing most probably to its rapid elimination.

The blood of an uninfected rat treated as above has also been used in the *in vitro* experiments recorded below.

Rats treated with Sodium Antimony Lactate and with Antimony Sodium Calcium Lactate.

Through the kindness of Messrs. von Heyden we have been enabled to make some experiments with the above compounds. The sodium antimony lactate contains 26 per cent. of antimony,

* 'Roy. Soc. Proc.,' B, vol. 80, p. 487.

and the antimony sodium calcium lactate 17 per cent., so they are both much weaker in antimony than the tartrates which we have used. By the addition of a small quantity of laetic acid we were able to get a 1 per cent. solution of both salts, and in this strength the solutions were not very irritating, but neither with rats nor with larger animals are they as effective as the tartrates or the metal.

The following table shows the results obtained with sodium antimony lactate 1 per cent.

Average duration of untreated disease 6·9 days :—

Rats of 150 to 200 Grammes Weight.	Number of Doses, and Quantity.	Recur- rences.	Lived.	Remarks.
1	2 of 4 minims	0	9 days	Died from enteritis.
2	4 of 4 "	0	20 "	Died from retained foetus.
3	4 of 4 "	1	37 "	
4	5 of 4 "	1	46 "	
5	6 of 4 "	2	100 "	
6	4 of 5 "	0	74 "	} (No trypanosomes found in any of these rats after death.)
7	5 of 5 "	1	48 "	

The following table shows the results obtained with antimony sodium calcium lactate 1 per cent.

Average duration of untreated disease 6·9 days :—

Rats of 150 to 200 Grammes Weight.	Number of Doses, and Quantity.	Recur- rences.	Lived.	Remarks.
1	3 of 4 minims	1	83 days	No trypanosomes found <i>post-mortem</i> .
2	4 of 4 "	0	25 "	Living trypanosomes found <i>post-mortem</i> .
3	5 of 4 "	2	68 "	No trypanosomes found <i>post-mortem</i> .
4	6 of 4 "	2	45 "	" " "
5	5 of 5 "	2	64 "	" " "
6	6 of 5 "	2	68 "	" " "
7	8 of 5 "	2	57 "	" " "
8	4 of 7 "	0	131 "	" " "

On dogs the effect was very much less marked than on rats, and an effective dose became inconveniently large.

The following experiments show the relatively greater time taken for these salts to act, as compared with the sodium or lithium antimony tartrates, which drive all the trypanosomes from the peripheral blood in about an hour after the dose.

A Surra rat was taken on the fourth day, when the trypanosomes are numerous in the blood, and 5 minims of a 1 per cent. solution of sodium antimony lactate were injected.

Blood was taken			and showed the following:
$\frac{1}{2}$ hour after injection...			Trypanosomes affected by the drug: are extremely active, and show a tendency to swell.
1	„	„	... Very few normal trypanosomes to be seen: nearly all are swollen and spherical in shape (=“ battledores ”). Still large numbers.
$1\frac{1}{2}$ hours	„	„	... Much smaller number of trypanosomes to be seen: a few “ battledores ”: a few motionless ones, and one or two normal forms.
2	„	„	... “ Battledores ” have all disappeared: one or two slowly moving normal forms seen.
$2\frac{1}{2}$	„	„	... Ditto.
$3\frac{1}{2}$	„	„	... No trypanosomes found.

A similar experiment made with a rat treated with antimony sodium ealeium lactate yielded praetieally the same result. Further experiments made with these drugs *in vitro* will be mentioned later.

Experiments made with Antimony (Metal in state of finest Division) suspended in various Oily Media.

Since the curative results following treatment with the metal antimony* suspended in Colonel Lambkin's medium seemed promising, many trials have been made with the metal suspended in other oily media, such as olive oil, cod liver oil, lanolin, egg-yolk, &c., in order, if possible, to obviate, or at any rate reduce, the extremely irritating properties of the metal, which seriously interfere with its practical use.

In olive oil a 5 per cent. suspension was used: with one dose of 3 minims Surra rats lived for 15 days, and died with living trypanosomes in their blood. Seventeen Surra rats were given one dose of 5 minims on the fourth day of the disease, and they lived from 41 to 133 days: in these there were no recurrences, nor were trypanosomes found after death, and sub-inoculations were in every case negative. Six Surra rats were treated with the same dose in order to observe the time taken for the complete disappearance of the trypanosomes from the blood.

Blood was taken			and showed the following:
$\frac{1}{2}$ hour after injection...			Trypanosomes very active.
1	„	„	... As numerous: show evidences of swelling.
$1\frac{1}{2}$ hours	„	„	... Still numerous: nearly all swollen: some “ battledores.”
2	„	„	... Very few forms found: all “ battledores.”
$2\frac{1}{2}$	„	„	... No trypanosomes seen.

* ‘Roy. Soc. Proc.’ B, vol. 80, p. 483.

Two Surra rats were taken on the fifth day, when the blood was swarming with trypanosomes, and 6 minims were given. Two and a-half hours after the rats were killed, and smears were made from the lungs, liver, spleen, kidney, bone-marrow, heart's blood, and brain. In none of the specimens could a trypanosome be found after prolonged examination.

This oil was also given to several rats upon recurrences after treatment with small doses of the lactates mentioned above: in these cases the effect was much less marked, even although the number of trypanosomes in the blood was much less than in the rats treated for the first time. This accords with our general experience that recurrences are much more difficult to deal with than the initial infection, and this applies to all the drugs we have tried.

A suspension in cod liver oil took four hours to drive the trypanosomes out of the peripheral blood.

The suspension in egg-yolk appeared to act in rats better than any other; in dogs, however, the results were variable; sometimes strikingly good, at others no better than the other mixtures: sometimes causing great irritation and sloughing, sometimes not causing any irritation at all. We have rats alive for more than 120 days after inoculation, with no recurrences, after one dose.

An experiment was made to see how long one dose took to drive the trypanosomes out of the blood. A Surra rat on the fourth day was treated with 5 minims of a 5 per cent. suspension.

Blood was taken and showed the following:

$\frac{3}{4}$ hour after injection...	Trypanosomes much affected, but not decreased. Many "battledore" forms.
$1\frac{1}{4}$ hours ,, ...	Trypanosomes reduced in numbers: all swollen and "battledore" forms: very little movement.
$2\frac{1}{2}$,, ,, ...	No trypanosomes found.

Experiments with Quassia.

Dr. Guillemard, of Cambridge, suggested that quassia, on account of its known poisonous effects on some of the lower forms of life, should be tested for its trypanocidal qualities. A series of experiments was therefore undertaken on rats.

Six Surra rats were treated on the third and following days of the disease with a 5 per cent. solution of the pharmacopœal extract of quassia: they were given three doses subcutaneously—5 minims on the third day, 10 minims on the fourth, and 10 minims on the fifth day. The trypanosomes were entirely unaffected, and the animals died on the sixth—seventh day. Another series of 12 Surra rats was treated with a two hours' decoction of quassia-wood made with the minimum amount of water. Of this three doses were given—5 minims on the third day and 10 minims on the fourth and fifth days. The trypanosomes in these rats were also entirely unaffected, and the animals

died on the sixth—seventh day. It was also tried intravenously in rabbits in doses of 30 minims of the decoction: no effect was produced, and the rabbits died on or about the 42nd day.

Experiments made *in vitro* correspond with these results, and will be described later.

Experiments with Arsenophenylglycin.

Professor Ehrlich kindly sent some of this substance to Dr. Bagshawe, the Director of the Sleeping Sickness Bureau, with which we have made some initial experiments upon rats. Ehrlich found that Nagana mice could be cured, in practically every case, with this substance. But the effects on larger animals, so far as we have gone, are not quite so satisfactory, and it compares in this undesirable manner very well with the antimony tartrates, with which we can cure practically every case of Surra in rats, but which do not have anything like the corresponding effects on rabbits, guinea-pigs, and dogs. It is not only in the question of practical dosage that difficulties arise: each kind of animal has a personal equation, and their reaction to a given drug is not similar. This, and the relatively larger dosage in bigger animals, present considerable practical difficulties in the treatment of trypanosomiasis.

Our experiments have given the following results. Out of eight Surra rats of 180 to 200 grammes weight which were given one dose of 25 minims of a 1 in 80 solution of arsenophenylglycin, four died on the 19th day with living trypanosomes in their blood, the recurrences having taken place on the 16th—17th day. Two were given three and five doses respectively of 5 minims of a 1 per cent. solution of lithium antimonyl tartrate on the 17th and following days, and they lived 59 and 51 days. Of the two which are still living (95 days), one has had five doses of 5 minims of a 1 per cent. solution of lithium antimonyl tartrate, beginning on the 17th day, and the other had one similar dose given on the day before the recurrences occurred in the other rats.

The following experiment shows the effect of this substance upon the trypanosomes in the blood, and how much longer it takes than the antimony salts to produce its effects.

A Surra rat on the fourth day of the disease was treated with 1 c.c. of a 2 per cent. solution of arsenophenylglycin (practically the same dose as given to the other rats).

Blood was taken			and showed the following:
$\frac{1}{2}$ hour	after injection...	Trypanosomes showed slight increase of motility.	
1	„ „	... Ditto.	
2	hours „	... Ditto, but more marked.	
3	„ „	... Trypanosomes not quite so active and fewer in number.	
4	„ „	... Trypanosomes now very few in number.	
$4\frac{1}{2}$	„ „	... Only one or two trypanosomes to be seen in a preparation.	
5	„ „	... No trypanosomes seen.	

In these specimens no swollen, breaking up, or "battledore" forms were seen: the trypanosomes simply disappeared.

On the Effects of the Drugs used upon the Trypanosomes in the Living Body.

In studying the therapeutic effect of the various drugs tried, including metallic antimony in a state of finest division, repeated observations of the peripheral blood were made in order to observe the effect of the drug upon the trypanosomes, and to ascertain when the trypanosomes entirely disappeared from the blood. The first stage noticed of the effect of the drug was a great increase in the motility of the trypanosomes, followed by a gradual slowing down to movements slower than normal. At this stage there is a tendency for the whole trypanosome to swell, and to become bloated in appearance. The swelling of the trypanosome continues until it becomes almost spherical in form, or oftener "battledore" shaped; the protoplasm becomes indistinct, and the flagellum appears to be attached to only one side of the periphery; the macro-nucleus is fairly distinct, but it eventually breaks up, and then the swollen mass disintegrates. The spleen at this time is full of these broken up masses of trypanosomes, and as the nuclei will still stain, a plasmodial appearance is seen in films of bits of nuclei dotted about in a granular ground. These stages can be observed after treatment with all the salts of antimony used, and are well marked after the administration of the metal, in which case, however, the stages are slower. The soluble salts, lithium and sodium antimonyl tartrates, effect the total disappearance of the trypanosomes in about one hour. Metallic antimony, when given in the various media tried (Lambkin's medium, olive oil, cod liver oil, heavy paraffin oil, egg-yolk), brings about this disappearance in from two-and-a-half to four hours, according to the medium used; the first noticeable effects being produced in about half an hour. In the case of egg-yolk and olive oil the blood is free from trypanosomes in two-and-a-half hours. This would seem to show that some portion of the metal introduced must be changed into some soluble form very rapidly; but, apparently, after the reaction of the tissues occurs the antimony becomes more or less shut off, and absorption must take place very slowly, as traces of the metal, apparently unaltered, have been found as late as six to seven weeks after the injection.

Sodium antimony lactate and antimony sodium calcium lactate were found to act rather more slowly than the above (see Table above), the time at which the trypanosomes had completely disappeared varying from three to four hours.

It was noticed in these experiments that trypanosomes, though obviously drug-affected when the blood was taken, remained alive on the slide outside the body for a long time after all forms had disappeared from the circulating blood.

Further details of the time taken for the various drugs to act will be found in the sections upon sodium antimony lactate, antimony oil, antimony egg-yolk, and arsenophenylglycin.

On the Action of Trypanocidal Substances in vitro.

Experiments have been carried out with a view of throwing light on the more exact nature of the changes which are produced in trypanosomes when they are brought into contact with trypanocidal substances. The general principles we have observed in these experiments have been:—1. To dissolve the drug in some fluid so that when it is added to the infected blood it will not cause osmosis to occur in the cellular elements of, or trypanosomes contained in the blood. (The various substances were dissolved in a 0.89 per cent. salt solution, isotonic with rat's blood which was used in these experiments.) 2. To use always equal volumes of the solution and of the affected blood. 3. To use blood at the time when the trypanosomes are just becoming very numerous, so as to avoid the presence of old, feebly moving forms, which are always present in the later stages of an acute infection. The method of observation has been to watch the behaviour of the trypanosomes when in contact with the various solutions of the drug under the microscope. A measured drop of blood and of the solution are mixed on a slide with care; the mixed drop is then covered with a sufficiently large cover glass, and this is sealed with vaseline.

It has been found possible in this manner to exactly determine the dilutions at which the various drugs used cease to have an instantaneously trypanocidal action; further, in higher dilutions, by carefully watching the changes taking place in the trypanosomes, it is possible to determine the dilution at which no effect is produced, and between these two points the periods of time necessary to ensure immobility and death of the trypanosomes can be ascertained. By a comparison of the results obtained a very good estimate of the probable action of any drug when given to an affected animal can be arrived at.

For instance, sodium and lithium antimonyl tartrates were found to act, in the same dilutions, in a manner fairly comparable to their antimony content, and to their action on the trypanosomes in an affected animal. Again, with atoxyl a much higher concentration of the drug was necessary—it had to be about ten times stronger—in order to obtain the same destruction pictures, results corresponding with the rapidity of the disappearance of trypanosomes from the peripheral blood of affected animals when treated with the above drugs.

In the case of the two new lactates mentioned above, their therapeutical value was accurately foretold by a preliminary study of their action *in vitro* in the manner described. In all these experiments controls have been carried out; it has been found that trypanosomes will live and retain their activity for hours when infected blood and the diluting fluid alone are mixed together.

The various changes taking place in trypanosomes on coming into contact with a dilute trypanocidal drug, commencing with their preliminary extraordinary increase of activity, and their subsequent swelling up, immobility and disintegration, can be watched in all their different stages in this manner. These effects resemble very closely the changes which take place in the trypanosomes in the peripheral circulation of an animal treated with antimony.

The following tables show the effects produced by the different substances in their various dilutions.

Dilutions of sodium antimonyl tartrate in 0·89 per cent. salt solution mixed with Surra rat's blood, in equal parts. The control in all cases is equal parts of blood and 0·89 per cent. salt solution.

Dilutions.				Time.	Control.
1—500.	1—1,000.	1—5,000.	1—10,000.		
Motionless	Motionless	Few active forms.	Trypanosomes active.	1 min.	Very active.
"	"	Motionless	Few active forms ; rest sluggish.	10 mins.	"
"	"	"	All sluggish ...	30 "	"
"	"	"	Motionless ...	1 hour.	"

Dilutions of lithium antimonyl tartrate in 0·89 per cent. salt solution mixed with Surra rat's blood, in equal parts.

Dilutions.					Time.	Control.
1—500.	1—1,000.	1—5,000.	1—10,000.	1—20,000.		
Motionless.	Motionless.	Some active trypanosomes.	Active trypanosomes.	Very active trypanosomes.	1 min.	Very active.
"	"	Motionless	Some active trypanosomes.	Many active trypanosomes.	10 mins.	"
"	"	"	Practically no motile trypanosomes seen, only 1 or 2 in a slide. Tendency to clump.	Few active trypanosomes seen. Tendency to clump.	30 "	"
"	"	"	Motionless ...	1 or 2 active forms seen. Rest motionless.	1 hour	"

In a dilution experiment with lithium antimonyl tartrate made with the blood of a Surra rat after a second recurrence,

after treatment with antimony (metal) and on first recurrence with lithium antimonyl tartrate, the trypanosomes *in vitro* appeared to have a greater resistance to the dilute drug than the stock strain.

A comparison of the following table with the previous one will demonstrate this:—

Dilutions.								Time.
1—1,000.				1—500.				
A few active forms present...				A number of active forms present...				1 min.
Motionless				A few active forms seen				10 mins.
"				Motionless				30 "

This bears out our experience that the recurrences become less and less amenable to antimony as they increase in number.

The following table shows the action of atoxyl and lithium antimonyl tartrate compared in the above manner:—

Dilutions of Atoxyl.			Time.	Dilutions of Lithium Antimonyl Tartrate.		
1—500.	1—1,000.	1—5,000.		1—500.	1—5,000.	1—10,000.
Trypanosomes, all active.	Active ...	Active	1 min.	Trypanosomes, all motionless.	All markedly affected.	All fairly active.
Active, but affected.	" ...	"	5 mins.	Motionless; commencing disintegration.	Motionless	Less active.
Less active ...	Sluggish, but still many active.	"	15 "	Only <i>débris</i> seen.	"	Some still moving; tendency to clump.
Practically motionless.	Nearly all motionless; 1 or 2 active forms seen.	Many moving still.	2 hrs.	"	Disintegrated.	Motionless; some disintegration.

Concentrated decoction of quassia in 0·89 per cent. salt solution mixed with Surra rat's blood in equal parts.

Dilutions.				Time.	Control.
1—500.	1—1,000.	1—5,000.	1—10,000.		
Very active...	Very active	Very active	Very active	1 min.	Very active.
" ...	"	"	"	10 mins.	"
" ...	"	"	"	30 "	"
" ...	"	"	"	1 hour	"
Less active...	Less active	Less active	Less active	2 hours	Less active.

The conditions of the dilutions and the control were precisely similar at the end of two hours. There was no swelling nor clumping.

Dilutions of arsenophenylglycin in 0.89 per cent. salt solution mixed with Surra rat's blood in equal parts.

Dilutions.					Time.	Control.
1—100.	1—500.	1—1,000.	1—5,000.	1—10,000.		
Very active ...	Very active.	Very active.	Very active.	Very active.	1 min.	Very active.
Irritated: movements rapid and convulsive.	Activity increased.	"	"	"	10 mins.	"
Nearly motionless.	Sluggish	"	"	"	30 "	"
Motionless ...	"	"	"	"	1 hour	"

Experiments in vitro performed with the Blood of a Normal Rat which had been treated with Antimony.

Experiments were made in order to ascertain whether the blood of a rat which had been treated with antimony would show any active trypanocidal powers *in vitro*. Although in the case of an infected animal all the trypanosomes in the peripheral blood would have been destroyed in about an hour, no noticeable trypanocidal effects were shown by the blood of a treated rat in the following experiments.

A normal rat had 5 minims of a 1 per cent. solution of lithium antimonyl tartrate injected subcutaneously; its blood was taken at 15, 30, 60, and 70 minutes after the injection, and was mixed with an equal quantity of blood from a Surra rat containing many trypanosomes; the mixed bloods, taken at the times mentioned, were examined under the microscope at various intervals from 5 to 30 minutes after the mixing, and the trypanosomes were found to be entirely unaffected, so that the blood of the treated normal rat did not have any trypanocidal effect added to it by the dose of lithium antimonyl tartrate. The Surra rat, whose blood was used for this experiment, was then given 5 minims of a 1 per cent. solution of lithium antimonyl tartrate:—

Blood was taken		and showed the following:	
10 minutes after infection ...	Trypanosomes affected: movement very rapid.		
20 " "	... Many "battledores."		
40 " "	... Trypanosomes greatly decreased in number all "battledores."		
60 " "	... Blood quite free from trypanosomes.		

A normal rat was given four doses subcutaneously, one every other day, of 5 minims of a 1 per cent. solution of lithium anti-

monyl tartrate; 24 hours after the last dose a drop of its blood was mixed with a drop of blood from a Surra rat in which trypanosomes were plentiful. The mixture was watched under the microscope for half an hour, but no effect was produced; the blood of the treated animal behaving just as the blood of the control, an untreated rat.

A normal rate was given subcutaneously 10 minims (a lethal dose) of a 1 per cent. solution of lithium antimonyl tartrate, and its blood was mixed at half an hour, one hour, and one-and-a-half hours after the injection with an equal part of an emulsion of trypanosomes prepared from the lungs, liver, and heart's blood of a Surra rat just dead. Each of the mixtures was examined up to 30 minutes, but no effect whatever was produced on the trypanosomes. These experiments may be compared with those recorded on p.

Experiments with Antimony upon Dogs.

Since the date of the last paper a large number of experiments have been made with antimony in various forms upon dogs suffering from Surra. Of the five dogs mentioned there, one remains alive and well at the present date, more than a year after inoculation.

Our experiences with dogs show that they are extremely susceptible both to the disease and also to antimony: they are therefore not quite suitable animals for these experiments, although they have all lived many times the length of the untreated disease, that is 14 days. Five of the dogs were treated with small doses of sodium antimonyl tartrate in their drinking water, but the disease is so acute in dogs that this method of giving the drug, although it appeared to have some effect in postponing the reappearance of the trypanosomes in the blood, did not produce results sufficiently encouraging to warrant further experiments.

With regard to the experiments made with metallic antimony suspended in egg-yolk, the initial experiment was so encouraging as to make a further trial necessary. In this case the dog at the first relapse was given 20 minims of a $2\frac{1}{2}$ per cent. suspension: there was no local reaction, which in dogs is of frequent occurrence after the administration of antimony in any form, and the trypanosomes, which were very numerous, were entirely absent from the blood in 24 hours; the dog remained quite free from them for 48 days, and gained 3 lbs. in weight, and appeared perfectly well. The recurrence was very sudden, as the dog was perfectly well up to the moment when he was seized with a series of fits which ushered in the recurrence, from which he did not recover. A rat treated at the same time as this dog with 5 minims of the same suspension is alive and well more than 100 days after this one dose.

Many of the dogs mentioned in the table below have died with fits and paralyses and other nervous symptoms, but we are not

certain whether these are due to the disease or to the antimony. In certain of the dogs the treatment has appeared to alter the acute disease into a chronic one, and in one of these more chronic cases there was a considerable excess of cerebro-spinal fluid and a cellular exudation around the vessels in the brain, very similar in incidence and extent to that described and figured by one of us in rats dead from infection with *Trypanosoma gambiense*.*

There is a curious uncertainty in the local effects produced in dogs by antimony, whether injected subcutaneously or intramuscularly, and they vary from time to time in the same dog; sometimes little or no effect is produced, and sometimes the suppuration and necrosis produced are sufficient to kill the animal.

We have recently given 24 injections of lithium antimonyl tartrate subcutaneously to three dogs in the greatest possible dilution; of these three places have suppurated slightly, although the conditions under which they were given were similar to those under which the 21 other doses were given. (These dogs are now living and well 53 days after inoculation, and they have had no recurrences.)

The following table gives a synopsis of the treatment, &c., of Surra dogs:—

* 'Roy. Soc. Proc.,' B, vol. 79, p. 95.

Average Duration of Untreated Disease, 14 days.

No.	Weight, in Kilos.	Number of Doses.	Quantity of Dose, in Minims.	Material.	Recur- rences.	Remarks.
1	11	2	20	5 per cent. ant. cream ...	2	<i>Dog is alive and well 373 days after inoculation.</i>
2	11	2	20	" sod. ant. tart. ...	3	Died on 94th day : no trypanosomes found for 21 days before death. There were 41 days between the first and second recurrences. Died with fits and nervous symptoms.
3	18 $\frac{3}{4}$	4	20	" lith. ant. tart. ...	6	Died on 67th day. No trypanosomes found for 22 days before death. Died with fits and nervous symptoms.
4	8	3	12	sod. ant. tart. cream ...	4	Died of distemper on 63rd day. No trypanosomes found for 7 days before death.
5	6 $\frac{3}{4}$	3	10	" ant. cream. ...	3	Died of pneumonia on the 53rd day. No trypanosomes found for 11 days before death.
6	6 $\frac{1}{4}$	5	10	" lith. ant. tart. ...	1	Died from abscess on the 40th day. No trypanosomes found for 17 days before death.
7	7 $\frac{1}{4}$	5	10	" sod. ant. tart. ...	3	Died from abscess on the 61st day. No trypanosomes in blood for 10 days before death.
8	14 $\frac{1}{2}$	4	12	" lith. ant. tart. ...	2	Died on 55th day with fits and nervous symptoms. Trypanosomes in blood. Antimony given in water also.
9	12 $\frac{3}{4}$	2	15	" ant. oil. ...	2	Died on 77th day from abscess. No trypanosomes seen for 16 days before death. Antimony given in water also.
		1	20	" lith. ant. tart. ...		

No.	Weight, in Kilos.	Number of Doses.	Quantity of Dose, in Minims.	Material.	Recur- rences.	Remarks.
10	13½	2	12	5 per cent. ant. oil.	...	Died on 63rd day with nervous symptoms and paralysis. No trypanosomes found. Antimony given in water also.
		1	20	" lith. ant. tart.		
		2	15	" "		
11	8½	3	20	" ant. sod. lact.	...	Died on the 66th day with nervous symptoms. No trypanosomes found after death. Antimony given in water also.
		1	15	" lith. ant. tart.		
		1	10	" ant. oil.		
		1	15	" "		
		1	5	" "		
		2	2½	" "		
		2	15	" "		
		1	20	" "	...	
12	10	2	10	" "	3	Died on the 65th day with living trypanosomes in blood. Antimony given in water also.
		2	15	" "		
		4	15	" lith. ant. tart.		
		1	20	" "	...	
13	11½	1	15	" ant. oil.	1	Died on the 60th day with nervous symptoms. No trypanosomes seen for 29 days before death.
		1	15	" "		
		2	2½	" "		
		1	15	" "		
		1	20	" "		
		2	15	" "	2	Died on the 52nd day from abscess. No trypanosomes found after death.
14	10½	1	20	" "	...	
		1	15	" "		
		1	20	" lith. ant. tart.		
		2	15	" "	...	
15	13¾	1	15	" ant. oil "	5	Died on the 50th day with living trypanosomes in blood.
		2	20	" "		
		3	20	" lith. ant. tart.		
16	9¾	1	15	" "	0	Died on the 64th day from abscess. No trypanosomes found after death and no recurrences.
		2	15	" ant. oil.		
		1	10	" egg ant.		
		2	15	" ant. oil "	0	Died on the 48th day from pneumonia. No trypanosomes found after death.
17	9¼	1	15	" lith. ant. tart.	...	

18	9 $\frac{1}{4}$	1	15	2	"	"	...	1	Died on 50th day, possibly from ant. sod. lactate. No trypanosomes found after death.
19	10 $\frac{1}{4}$	2	15	5	"	aut. oil.	...	3	Died on 74th day with nervous symptoms. There were 48 days between the first and second recurrences.
		1	20	2	"	ant. sod. lact.	...		
		1	20	5	"	lith. ant. tart.	...		
		1	15	5	"	"	...		
		1	10	5	"	"	...		
		1	20	5	"	ant. cream.	...		
		1	20	2 $\frac{1}{2}$	"	egg ant.	...		
20	7 $\frac{1}{4}$	3	15	2 $\frac{1}{2}$	"	"	...	—	Trypanosomes practically never out of blood. Died on the 37th day, paralysed.
21	13 $\frac{1}{4}$	1	15	5	"	"	...	—	Trypanosomes practically never out of blood. Died on the 44th day with fits and nervous symptoms.
		2	10	2 $\frac{1}{2}$	"	"	...		
		3	20	5	"	"	...		
22	8 $\frac{1}{4}$	1	15	2	"	lith. ant. tart.	...	—	Trypanosomes practically never out of blood. Died on the 55th day with fits and nervous symptoms.
23	13 $\frac{1}{4}$	3	15	2 $\frac{1}{2}$	"	egg ant.	...	3	Died on the 55th day with fits and nervous symptoms.
		3	15	2	"	lith. ant. tart.	...		
		1	15	5	"	egg ant.	...		
		2	20	5	"	egg ant.	...		
24	12 $\frac{1}{4}$	2	15	5	"	lith. ant. tart.	...	2	Died on the 64th day with living trypanosomes in the blood.
		4	5	5	"	"	...		
		1	15	5	"	egg ant.	...		
		1	20	5	"	"	...		
		1	15	5	"	lith. ant. tart.	...		
		1	10	5	"	"	...		
		5	5	5	"	"	...		
25	9 $\frac{3}{4}$	1	10	5	"	"	...	2	Died on the 56th day with nervous symptoms.
		1	20	5	"	egg ant.	...		
		1	5	5	"	lith. ant. tart.	...		
26	8	5	10	5	"	"	...	2	Died on the 47th day. Trypanosomes found in the cerebro-spinal fluid.
		1	20	5	"	egg ant.	...		
		5	5	5	"	lith. ant. tart.	...		

[Reprinted from the PROCEEDINGS OF THE ROYAL SOCIETY,
B. Vol. 81.]

33. THE DEVELOPMENT OF *TRYPANOSOMA GAMB- BIENSE* IN *GLOSSINA PALPALIS*.

By Colonel Sir DAVID BRUCE, C.B., F.R.S., Army Medical Service; Captains A. E. HAMERTON, D.S.O., and H. R. BATEMAN, Royal Army Medical Corps; and Captain F. P. MACKIE, Indian Medical Service. (Sleeping Sickness Commission of the Royal Society, 1908.)

(Received July 5, 1909.)

[PLATES 4 AND 5.]

The following experiment is so complete in itself that no apology is offered for publishing it by itself. In 1903 the Sleeping Sickness Commission of the Royal Society came to the conclusion that the carrying of infection from a sleeping sickness patient to a healthy person by the *Glossina palpalis* was a mechanical act, and required no previous development of the parasite within the fly. The Commission also held that the power of transferring the disease was lost to the fly 48 hours after it had fed on an infected person.

Koch and Stuhlmann, in German East Africa, described developing forms in *Glossina*, but did not succeed in infecting healthy animals by the injection of these forms.

Kleine, in German East Africa, at the end of 1908, succeeded first in showing that *Glossina palpalis* could convey *Trypanosoma brucei* some 50 days after the fly had fed on an infected animal.

It seems, at first, strange that this fact should have escaped notice for 15 years, and can only be accounted for by assuming that it is an event of the rarest for a fly to be found which fulfils the unknown conditions necessary for the development of the trypanosomes in its interior. If we assume that it is only one fly in a hundred or in a thousand in which this development takes place, then the difficulty of observing the phenomenon can be understood.

Take the following experiments, for example:—

Table I.—Flies caught in an Infected Area, kept for some days, and then fed on Healthy Animals.

Trypanosoma brucei—*Glossina morsitans*.

Expt.	Place.	Observer.	No. of Flies fed.	No. of times Flies fed.	No. of Days before Infection or under observation.	Result.
210	Zululand ...	Bruce ...	5	32	64	Negative.
242	" ...	" ...	30	11	56	"
232A	" ...	" ...	50	15	34	"

These experiments seemed to show that if flies caught in a highly infected district, into which a horse could not be taken even for a few hours without contracting nagana, are kept without food for a few days—say three to five—they are then incapable of conveying infection. This appeared to be a strong proof that the duration of infectivity in the fly was a short one, since, if this were not the case, 1 of the 85 flies ought to have been in a condition capable of infecting, having, of course, been infected at some previous date in the “fly country.” It may be repeated, that these flies were caught in a most highly infected district, so that if *Glossina morsitans* can remain infective for 50 or 60 days, 1 at least of the 85 ought to have been in the condition which made it capable of conveying the disease.

This development of the trypanosomes in the fly is strikingly like what occurs in the test-tube with Novy's medium. A thousand tubes are inoculated with *Trypanosoma brucei*: the trypanosomes all appear to die off, but 20 days afterwards a peculiarly resistant individual is found in one tube of the thousand, who has adapted himself to the new environment, and soon multiplies into myriads. What it is which enables this particular individual to adapt itself to such altered conditions is unknown. It is the merest speculation to call it a sexual act and pick stout forms as females and slender forms as males.

Again, because this late development of the trypanosomes enables a particular fly to remain infected for 100 days, or even possibly for the remainder of its life, it by no means follows that this is the usual method of infection. The mechanical transference of the disease is proved up to the hilt, and for every case which falls a victim to the rare late-infected fly, a thousand must be infected by direct mechanical transference.

SUMMARY OF THE EXPERIMENT WHICH FORMS THE SUBJECT OF THIS PAPER.

Before describing at length the experiment which forms the subject of this paper, we may summarise it as follows:—

1. On March 5, 1909, 60 *Glossina palpalis* caught on the lake shore were placed in two cages, 30 in each. The flies were fed on two infected monkeys for 2 days. They were then starved for 72 hours to get rid of mechanical transference. The following 5 days they were placed on a healthy monkey, and every successive period of 5 days, or thereabouts, on a fresh monkey, up to 86 days, when the experiment came to an end. The result was, that the first two monkeys remained healthy, but that all the following monkeys, up to 75 days, became infected with *Trypanosoma gambiense*.

2. If 7 days be deducted for the incubation period, then the flies first became infected 18 days after their first feed on an infected animal,

3. There is some evidence that among the 60 flies only 1 was infective. Fifty-four days after the beginning of the experiment each cage was placed on a separate monkey. Up to that time both the cages of flies had been fed on the same animal. Cage A contained, after 54 days, 11 flies. Cage B, 4 flies. Cage A continued to infect monkeys for 21 days more, making a total of 75 days. Cage B did not infect. Again, as was natural, the flies gradually died off during the experiment, and as each fly died it was carefully dissected and examined for trypanosomes. Not a single trypanosome of any kind whatever was seen in any dissected fly up to 75 days, when a fly died in Cage A which was found to be swarming with trypanosomes similar to *Trypanosoma gambiense*. After the death of this fly, Cage A ceased to be infective, and when the experiment was stopped the remaining flies were killed off and dissected, but among them not a sign of a trypanosome could be seen. In the same way the flies remaining in the non-infective Cage B were examined, with a similar negative result.

4. Here follows an interesting and unique observation. A tiny drop of fluid taken from the gut of the 75-day fly injected under the skin of a monkey gave rise to Sleeping Sickness after an incubation period of eight days. This, so far as we are aware, is the first time this has been recorded.

5. It will be seen from the detailed experiment that the flies were starved for three days between several of the experiments. This, of course, was to get rid of the fallacy of mechanical transference.

6. It may be said that perhaps these monkeys became infected by some other means than the flies in the cage—for example, by other biting flies, or by contact. To this it may be answered that there are more than 200 monkeys under observation here, sick and healthy. They are all examined twice a week, but during the last eight months not a single case of accidental infection has taken place.

DETAILS OF THE EXPERIMENT.

Experiment 663.

To ascertain if development of *Trypanosoma gambiense* takes place in the interior of *Glossina palpalis*, and if so, how long does the fly remain infective.

March 5, 1909.—Two batches of *Glossina palpalis* caught on the Lake shore, consisting of 30 flies in each batch, were fed on monkeys. Experiments 568 and 214, whose blood contained numbers of *Trypanosoma gambiense*.

March 6.—The flies again fed as on the 5th, to ensure that as many as possible should get a feed of the infected blood. Nearly all the flies fed on one or other occasion. The flies are kept in a moist atmosphere at 22° C.

The following table gives the principal details of the experiment:—

Table II.

Date.	Day of Experiment.	Procedure.	Result.		Remarks.
			Positive.	Negative.	
1909.					
Mar. 5	—	Flies fed on infected monkey.			
6	1	" " " " " "			
7	2	Flies starved 72 hours.			
8	3	" " " " " "			
9	4				
10	5				
11	6	Fed on Monkey 579 ...		—	
12	7				
13	8				
14	9				
15	10				
16	11	" " 651 ...		—	
17	12				
18	13				
19	14				
20	15				
21	16	" " 652 ...	+		
22	17				
23	18				
24	19				
25	20				
26	21	" " 653 ...	+		
27	22				
28	23				
29	24				
30	25				
31	26	" " 654 ...	+		
Apr. 1	27				
2	28				
3	29				
4	30				
5	31	" " 655 ...	+		
6	32				
7	33				
8	34				
9	35				
10	36	" " 672 ...	+		
11	37				
12	38				
13	39				
14	40	" " 722 ...	+		
15	41				
16	42	Starved for 72 hours.			
17	43				
18	44				
19	45				
20	46				
21	47	Fed on Monkey 727 ...	+		
22	48				
23	49				
24	50				
25	51				

Date.	Day of Experiment.	Procedure.	Result.		Remarks.
			Positive.	Negative.	
Apr. 26	52 }	Starved for 76 hours.			
27	53 }				
28	54 }				
29	55 }				
30	56 }	Cage A fed on Monkey 735	+		
May 1	57 }				
2	58 }				
3	59 }				
4	60 }	Starved for 74 hours.			
5	61 }				
6	62 }				
7	63 }				
8	64 }	Cage A fed on Monkey 749	+		
9	65 }				
10	66 }				
11	67 }				
12	68 }	Starved for 72 hours.			
13	69 }				
14	70 }				
15	71 }				
16	72 }	Cage A fed on Monkey 765	+		
17	73 }				
18	74 }				
19	75 }				
20	76 }	Starved for 72 hours.			
21	77 }				
22	78 }				
23	79 }				
24	80 }	Cage A fed on Monkey 764			
25	81 }				
26	82 }				
27	83 }				
28	84 }	Starved for 72 hours.			
29	85 }				
30	86 }				
31	87 }				
		Cage A fed on Monkey 848			
		Starved for 72 hours.			
		Cage A fed on Monkey 848			
		Starved for 72 hours.			
		Cage A fed on Monkey 911			
		Experiment stopped.			

Remarks on the Experiment.

Everyone will agree that this is a most interesting experiment. It is evident that a single infected fly did all the mischief, and by good luck this fly was detected. Captain A. E. Hamerton, D.S.O., had charge of the experiment at first, and on his leaving Mpumu about the beginning of May, it fell to Sergeant A. Gibbons, Royal Army Medical Corps. Both are to be congratulated on the results, which are the outcome of care and thoroughness. Captain F. P. Mackie had the good fortune to dissect the fly which did the injury, and which will be fully described later.

INCUBATION PERIOD.

From the experiment may be drawn the incubation period in monkeys bitten by a late-infected fly.

It is remarkable how regular this is in those monkeys which gave a positive result. This shows how very infective Fly 866 was. Apparently each time it bit it infected.

The following table gives the period of incubation in each case:—

Table III.

Date.	Experiment.	Flies first fed.	Trypanosomes appeared in Blood.	Number of Days before Trypanosomes appeared in Blood.
1909.		1909.	1909.	
March 19 ...	652	March 19 ...	March 30 ...	11
" 24 ...	653	" 24 ...	April 2 ...	9
" 29 ...	654	" 29 ...	" 6 ...	8
April 3 ...	655	April 3 ...	" 13 ...	10
" 8 ...	672	" 8 ...	" 15 ...	7
" 13 ...	722	" 13 ...	" 20 ...	7
" 18 ...	727	" 18 ...	" 24 ...	6
" 28 ...	735	" 28 ...	May 5 ...	7
May 5 ...	749	May 5 ...	" 11 ...	6
" 12 ...	765	" 12 ...	" 17 ...	5

Leaving out the first experiment, 652, as it is doubtful as to the exact day Fly 866 became infective, this gives an average incubation period of seven days. It would therefore appear that Fly 866 probably infected each animal on the first day it bit it, showing how dangerous such an infected fly is.

DESCRIPTION OF THE *Glossina palpalis*, FLY 866, WHICH WAS DISSECTED 75 DAYS AFTER HAVING FED ON A MONKEY WHOSE BLOOD CONTAINED *Trypanosoma gambiense*.

Experiment 866.

May 19, 1909.—Dissected a *Glossina palpalis*, which was found dead to-day in Cage A of Experiment 663. On removing the viscera by the usual method, the mid-gut was seen to be of a pale salmon-pink. A small quantity of its contents, examined in the fresh condition, was found to contain enormous numbers of trypanosomes. The tube of this part of the intestine was absolutely crammed with active, seething masses of these flagellates. In regard to the other parts of the fly, nothing was seen in the proboscis. In the proventriculus one trypanosome only was found. The salivary glands contained large numbers of altered-looking trypanosomes, the fore-gut many large stout forms, with bright granules. The crop was empty and showed nothing. The Malpighian tubules, hind-gut, and proctodæum also were drawn blank.

In addition to examining these organs in the fresh condition, smears were made and stained. The examination of these stained specimens gave the following results:—

The salivary glands.—These had been carefully removed before the intestine was opened, and therefore had no chance of being fouled. As will be seen from the coloured drawing (Plate 4, fig. 1), the trypanosomes found in these glands differed from

those seen in the intestine. The bodies are very irregular in shape, and contain, besides a reddish-stained nucleus, dark deeply-stained coarse chromatin granules. The other cell contents remain unstained. Free chromatin granules and flagella are to be seen scattered over the field. Sometimes the bodies are definitely pear-shaped, with a flagellum coming from the narrow end, and rarely a more definite trypanosome shape can be seen; but never a true trypanosome.

[It is a matter of deep regret that an inoculation experiment was not made with an emulsion of part of the salivary glands.]

The fore-gut.—The fore-gut contained many trypanosomes. The cytoplasm stains a pale blue, and the nucleus a reddish-purple. The micronucleus is not distinctly seen in some of the trypanosomes, but when it is, it is always distinctly posterior to the nucleus. The protoplasm contains many coarse darkly-stained chromatin granules. The undulating membrane is less marked than in the normal blood trypanosome, and the flagellum, which usually springs from a micronucleus-like body, is less deeply stained (Plate 4, figs. 6-13).

The mid-gut.—The mid-gut contained innumerable trypanosomes of the *gambiense* type. Some are dividing, and all have a well-marked nucleus and micronucleus, the latter at or near the posterior extremity. The protoplasm contains many chromatin granules, and an undulating membrane and flagellum are present (Plate 4, figs. 6-16). Many groups, or rosettes, composed of 15 to 20 individuals, occur, the flagella pointing outwards (Plate 5, fig. 1).

The *proboscis*, *proventriculus*, *thoracic gut*, *crop*, *hind-gut*, and *Malpighian tubes* contained no trypanosomes.

The most interesting thing in this description of the examination of Fly 866 is the condition of the salivary glands. How these trypanosome-like bodies, or derivatives of trypanosomes, got into them is a mystery, and we will content ourselves at present with merely placing the bare fact on record until the salivary glands of similarly infected flies are examined.

There is one fallacy which might be pointed out. It is assumed that Fly 866 became infected on the first or second day of the experiment. It is possible that it became infected when feeding on the fifth day on an animal which showed trypanosomes in its blood a day or two later. This, however, is unlikely, as no other fly showed trypanosomes on dissection.

In order to make the story more complete, on Plate 4, figs. 1-5, is represented the *Trypanosoma gambiense* from the blood of one of the monkeys on which the flies were fed at the beginning of the experiment, and on Plate 5, figs. 2-5, are shown *Trypanosoma gambiense* from the monkey which became infected from the contents of the mid-gut of Fly 866.

PROPORTION OF INFECTED FLIES TO NON-INFECTED IN NATURE.

In the experiment under consideration it is seen that, in artificially-infected flies, only 1 in 60 showed the phenomenon of late infectivity. In nature the proportion must be less, as many of the flies, in many places at least, can never have fed on an animal whose blood contained *Trypanosoma gambiense*.

That there can be but few under natural conditions Table IV. shows. The table is made by subtracting the flies fed on the animal during the last seven days, before trypanosomes were found in the blood, this being the incubation period, from the total number. The experiments consist in catching tsetse flies in the infected area, bringing them to the laboratory and placing them straightway on healthy animals.

The first two experiments were made with *Trypanosoma brucei* and *Glossina morsitans*, and it would appear from them that 104 and 108 flies were used respectively before an infective one was found. This perhaps explains why Bruce's 85 flies failed to infect.

Table IV.—Table to show Probable Number of Naturally Infected Flies per thousand.

Expt.	Place.	Observer.	No. of Flies fed before Infection took place.	Result.		Probable No. of Naturally Infected Flies per thousand.
				Posi- tive.	Nega- tive.	
TRYPANOSOMA BRUCEI—GLOSSINA MORSITANS.						
225	Zululand	Bruce	104	+		9.6
236	"	"	108	+		9.2
TRYPANOSOMA GAMBIENSE—GLOSSINA PALPALIS.						
94	Uganda ...	Bruce and Nabarro	89	+		11.2
130	" ...	Bruce, Nabarro, and Greig.	850	+		1.2
131	" ...	" " "	506	+		1.9
136	" ...	Nabarro and Greig	723		—	
228	" ...	Greig and Grey ...	866	+		1.2
301	" ...	" " " "	2,299		—	
45	Leopold- ville.	Dutton, Todd, and Hannington.	457		—	
46	"	" " "	552		—	
128 _A	River ...	" " "	25		—	
139	" ...	" " "	262		—	
141	" ...	" " "	52		—	
182	Kasongo	" " "	211		—	
198	"	" " "	2,659	+		0.4
203	"	" " "	1,789		—	
213	"	" " "	717		—	
52	Uganda ...	Bruce, Hamerton, Bateman, and Mackie.	41		—	
214	" ...	" " "	3,284	+		0.3
568	" ...	" " "	178	+		5.6
571	" ...	" " "	850	+		1.2
53 ^o	" ...	" " "	21		—	
612	" ...	" " "	615	+		1.6
674	" ...	" " "	2,315	+		0.4

^o Animal died.

In the experiments with *Trypanosoma gambiense* and *Glossina palpalis* the average is 2.5 per thousand. It is, of course, impossible to tell how many of these positive experiments were infected by mechanical transference or by a late-infective fly; but, in

any case, the proportion is small. If this were not so, all the native population of the Lake shore, and most of the Europeans in Uganda, would long ago have been blotted out.

DESCRIPTION OF PLATES.

PLATE 4.

Smear preparation of salivary glands of *Glossina palpalis*, Experiment 866, stained Giemsa, showing irregularly shaped trypanosomes, with unstained protoplasm, reddish-coloured nuclei, and deeply stained chromatin granules. Note the chromatin granules scattered singly about the field, each surrounded by a pale area, fig. 1. $\times 2000$.

Normal *Trypanosoma gambiense* from monkey, Experiment 568, on which the flies were fed at the beginning of the experiment, figs. 2, 3, 4, and 5. $\times 2000$

Trypanosomes from the mid-gut of infected fly, Experiment 866, figs. 6-16. $\times 2000$.

PLATE 5.

Rosette form from the mid-gut, fig. 1. $\times 2000$.

Trypanosoma gambiense from the blood of monkey, Experiment 868, into which a tiny drop of the contents of the mid-gut of Fly 866 had been injected, figs. 2-5. $\times 2000$.

Trypanosomes from the fore-gut of Fly 866, stained Giemsa, figs. 6-13. $\times 2000$.

[Reprinted from the PROCEEDINGS OF THE ROYAL SOCIETY,
B. Vol. 81.]

34. A NOTE ON THE OCCURRENCE OF A TRYPANOSOME IN THE AFRICAN ELEPHANT.

By Colonel Sir DAVID BRUCE, C.B., F.R.S., Army Medical Service; Captains A. E. HAMERTON, D.S.O., and H. R. BATEMAN, Royal Army Medical Corps; and Captain F. P. MACKIE, Indian Medical Service. (Sleeping Sickness Commission of the Royal Society, 1908.)

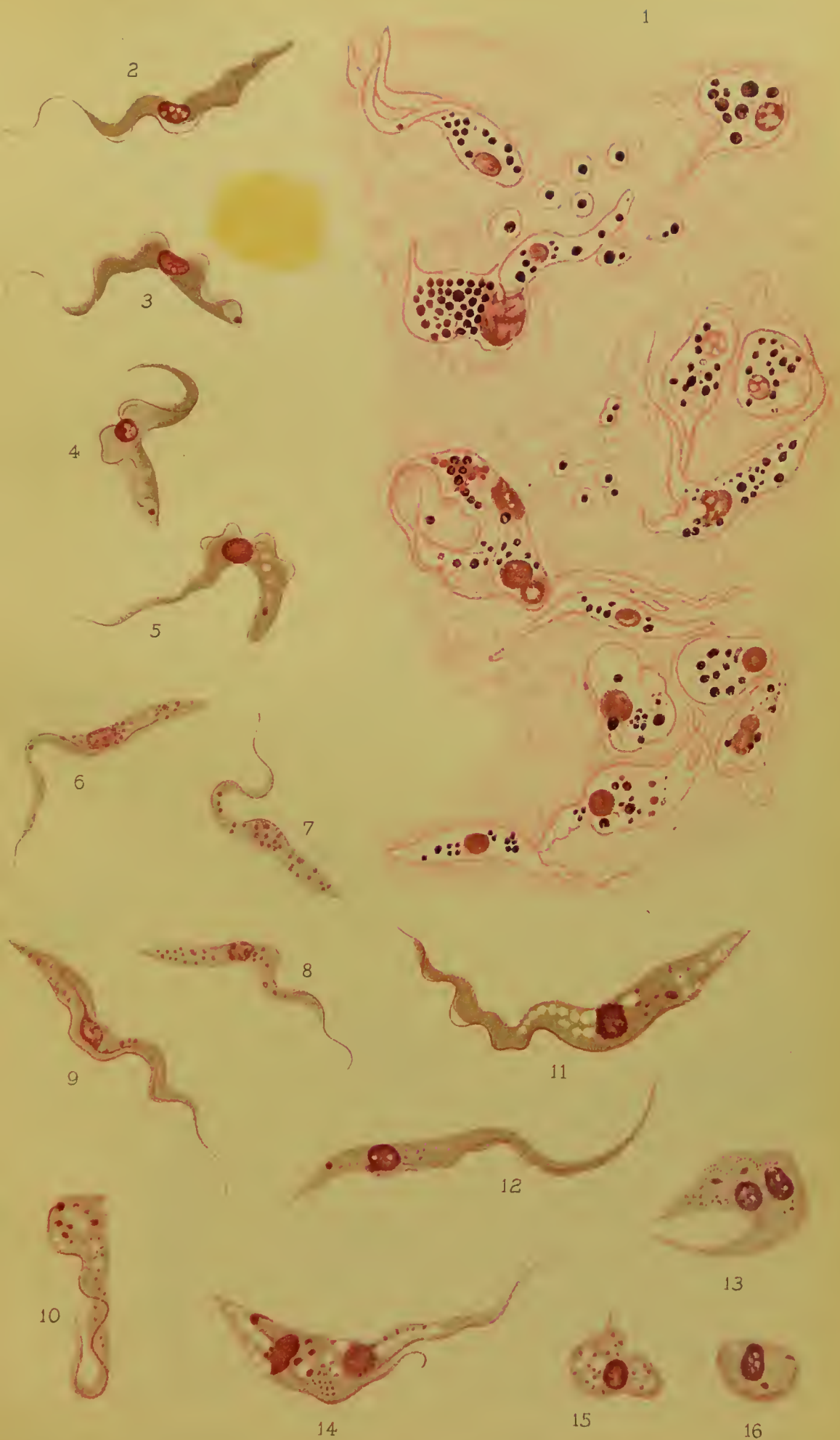
(Received July 5, 1909.)

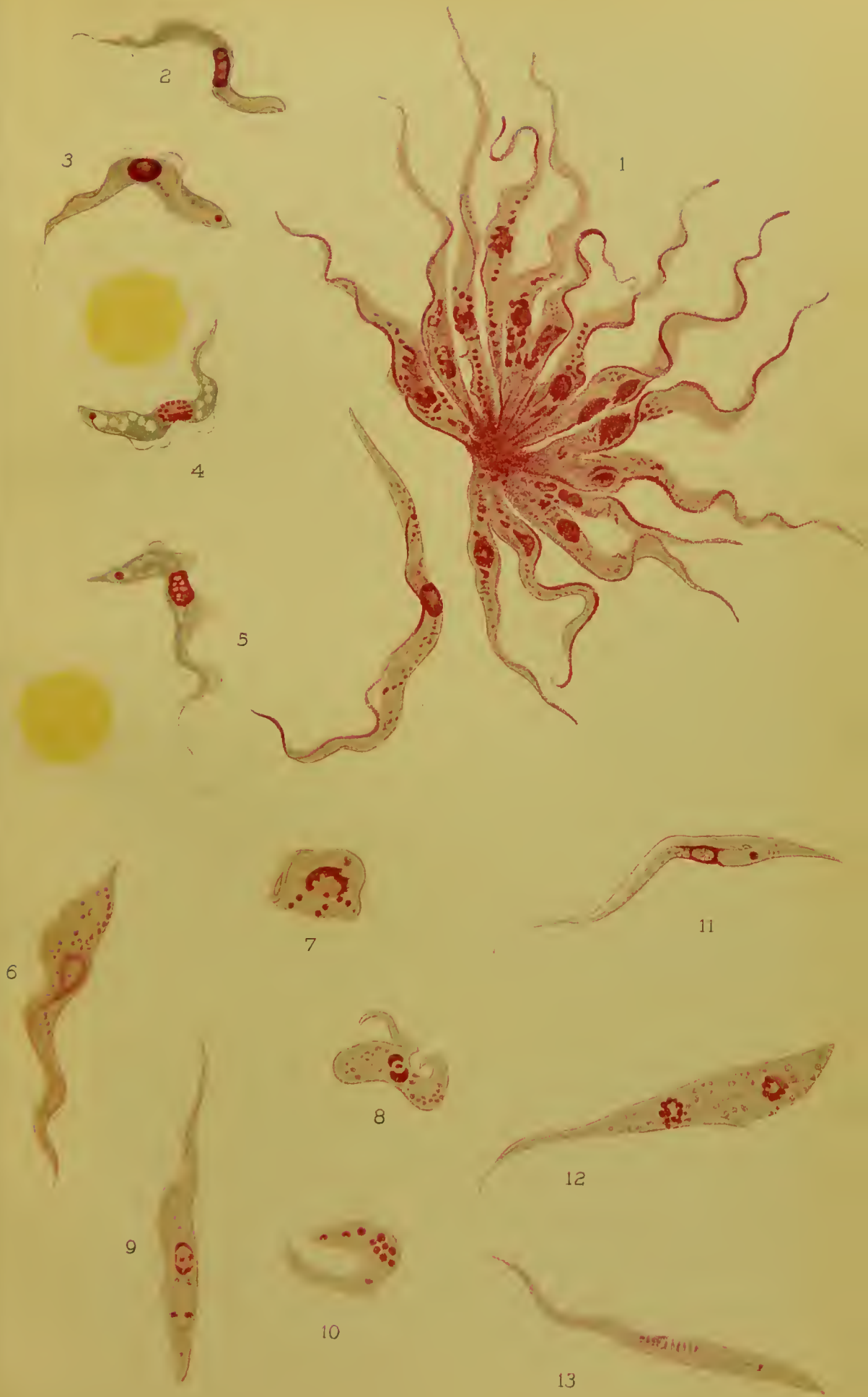
[PLATE 6.]

As trypanosomes have never been reported as having been observed in the blood of the African Elephant, the Commission thought it would be of interest to note this observation.

In Laveran and Mesnil's book on trypanosomes, translated by Nabarro, on p. 261 it is stated that "the occurrence of Surra (*Trypanosoma evansi*) in elephants in India and Burmah is practically proved. In this connection we have only the statement of G. H. Evans that, in 1893, 14 out of 32 elephants died of the disease in Burmah." The year 1893 is almost prehistoric for trypanosomes. At that time observers have even failed to distinguish between the common rat trypanosome—*Trypanosoma lewisi*—and that of Surra. It may well be, then, that Evans was mistaken in his diagnosis of the species causing this large mortality in elephants.

The African elephant, in whose blood this trypanosome was found, was shot by Mr. L. C. Lea-Wilson, of the Uganda Company, Limited, at a spot two miles from the eastern shore of Lake Albert, near Ngogole, about $31^{\circ} 10' \text{ E. lat.}$ and $1^{\circ} 30' \text{ N. long.}$







It is to be regretted that none of the blood was injected into a dog, donkey, or ox, in order that a fuller study of this trypanosome might have been made. As it is, all the material available are a couple of smears made by Mr. Lea-Wilson and sent to the Commission.

Morphology of the Trypanosome of the Elephant.

Method of Fixing and Staining.—The two slides received from Mr. Lea-Wilson were fixed in osmic acid vapour and alcohol, stained in Giemsa, and decolorised in orange tannin.*

Length.—For method of measurement see the same paper, p. 16. As will be seen from the coloured plate, which was drawn by Sergeant Gibbons, R.A.M.C., this trypanosome is of medium size. The average length of 18 individuals is 18·5 microns: maximum 21, minimum 15.

Breadth.—On an average the breadth at the thickest part is 3 microns.

Shape.—This trypanosome is of the *Trypanosoma brucei* type, inasmuch as it has a well-developed undulatory membrane and free flagellum. As will be seen from the drawing (Plate 6), one noteworthy feature it has is the uniformity in size and shape of the different individuals. The posterior end is blunt, or conical, reminding one somewhat of the head of a seal, with the bulging micronucleus for an eye. The body thickens as far as the middle, when it gradually tapers away to the anterior end.

Contents of Cell.—The protoplasm is clear and particularly free from granules.

Nucleus.—The nucleus is compact and sharply defined from the neighbouring protoplasm. In shape it is round, or oval, and often lies nearer the anterior extremity than the posterior. Its length averages 2 microns.

Micronucleus.—The micronucleus is small, round, and distinct. It is situated close to the posterior extremity, and often appears to bulge above the surface.

Undulating Membrane.—The undulating membrane is well developed and thrown into well-marked folds.

Flagellum.—The flagellum stains deeply. It runs from the micronucleus along the edge of the undulating membrane, beyond which it projects as a free flagellum for some 5 or 6 microns.

Conclusions.

In our present state of knowledge it seems impossible to name trypanosomes from their form alone. We were, however, much surprised, a short time ago, by Sir John McFadyean separating with ease *Trypanosoma brucei* from *Trypanosoma evansi*. If this can be done for such closely related species, surely it should be possible to do it for all. To assist to this end it would be well if observers would adopt one method of fixing, staining, and measuring. In the "Third Report of the Wellcome Research Laboratories," Khartoum, facing p. 30, there is a coloured plate of trypanosomes, stated to have a magnification of 1000. On measuring one of them it is found to have a magnification of

* Vide 'Roy. Soc. Proc.,' Series B, vol. 81, p. 16.

between 2000 and 3000. Then, again, many of the trypanosomes depicted are dividing forms, which is misleading.

The method of measuring must also make a difference. For example, in Laveran and Mesnil's book the length of *Trypanosoma brucei* in the rat is given as 26 to 27 microns, whereas by our method of measuring the average length of 20 individuals is 22·8 microns: maximum 25, minimum 20.

The trypanosome of the elephant has an average length of 18·5 microns: maximum 21, minimum 15, a well-developed undulatory membrane and free flagellum. The trypanosomes with free flagella are *Trypanosoma brucei*, *cazalboui*, *evansi*, *gambiense*, *pecaudi*, and *soudanense*. It probably is neither *Trypanosoma cazalboui* nor *pecaudi*, on account of its well-developed undulating membrane and uniform size. Under the circumstances it is impossible to decide as to its identity with *Trypanosoma brucei*, *gambiense*, or *soudanense*, but if a guess were hazarded then it would be *Trypanosoma soudanense*.

Until the nature of this species is better known we propose to name it *Trypanosoma elephantis*.

[Reprinted from the PROCEEDINGS OF THE ROYAL SOCIETY,
B. Vol. 82.]

35. SLEEPING SICKNESS IN UGANDA.—DURATION OF THE INFECTIVITY OF THE GLOSSINA PALPALIS AFTER THE REMOVAL OF THE LAKE-SHORE POPULATION.

By Colonel Sir DAVID BRUCE, C.B., F.R.S., Army Medical Service; Captains A. E. HAMERTON, D.S.O., and H. R. BATEMAN, Royal Army Medical Corps; and Captain F. P. MACKIE, Indian Medical Service. (Sleeping Sickness Commission of the Royal Society, 1908-09.)

(Received November 16,—Read November 25, 1909.)

During the last two years the policy of clearing the shores and islands of Lake Victoria of their inhabitants has been carried out by the Uganda Administration, with a view to the stamping out of Sleeping Sickness.

It will be remembered that the area of distribution of Sleeping Sickness and of the *Glossina palpalis* in Uganda is the same, and is limited to a narrow belt along the Lake-shore and islands. For the past two years no native has been allowed to live or work within two miles of the Lake-shore, except at a few cleared landing-places; and within the last few months all the islands have been emptied.

Until recently it was believed that the fly only retained its infectivity for 48 hours, and that it would, theoretically, be possible with safety to clear an island of its infected population one day and restock it with healthy natives a few days later. Recent work, however, has shown this to be wrong, since it has



been found by experiment that the fly can retain its infectivity up to 80 days. It is probable that after a fly has become infected it will harbour the trypanosomes for the rest of its life; but what the duration of this is, under natural conditions, is unknown.

From an administrative point of view, therefore, it is most important to find out how long the flies on the Lake-shore remain infective after the native population has been removed. Until this is known it will not be safe to allow the Lake-shore and islands to be re-inhabited.

As soon as the Sleeping Sickness Commission of the Royal Society reached Uganda experiments were begun to test this point. At first the flies were collected at Kibanga, a cleared landing-place in Buka Bay, six miles from the laboratory. This landing-place was used as a market, where the inhabitants of the Island of Buvuma came once a week to trade with the natives on the mainland. In November, 1908, Kibanga had become somewhat overgrown, and tsetse flies were present in some numbers. As the Buvuma islanders were highly infected with Sleeping Sickness, this constituted a danger to the healthy natives of the mainland, who had come to the market from outside the Sleeping Sickness area. Steps were at once taken to have the landing thoroughly cleared of undergrowth, with the result that in a short time the flies disappeared.

The following experiment shows the result:—

Experiment 52.—Monkey.

To ascertain if *Glossina palpalis* caught at Kibanga market-place are capable of giving rise to Sleeping Sickness in a healthy monkey.

Date.	No. of Flies.		Trypano- somes.	Malaria.	Date.	No. of Flies.		Trypano- somes.	Malaria.
	Put on.	Fed.				Put on.	Fed.		
1908.					1908.				
Nov. 3	—	—	—	+	Dec. 6	—	—	—	+
" 6	—	—	—	+	" 7	—	—	—	+
" 14	15	12	—	+	" 15	—	—	—	+
" 16	17	17	—	+	" 17	1	1	—	+
" 17	7	7	—	+	" 18	—	—	—	+
" 18	4	1	—	+	" 23	—	—	—	+
" 19	7	4	—	+	" 26	—	—	—	+
" 20	—	—	—	+	" 30	—	—	—	+
" 22	50	34	—	+					
" 23	—	—	—	+	1909.				
" 24	—	—	—	+	Jan. 4	—	—	—	+
" 25	—	—	—	+	" 9	—	—	—	+
" 27	—	—	—	+	" 18	—	—	—	+
" 29	—	—	—	+	" 20	—	—	—	+
" 30	—	—	—	+	" 26	—	—	—	+
Dec. 2	10	7	—	+	" 28	—	—	—	+
" 3	12	5	—	+	Feb 6	—	—	—	+
" 4	5	3	—	+	Mar. 1	—	—	—	+

Remarks.—The result of this experiment is negative. The

number of flies caught is small, and they soon disappeared as the clearing of the place proceeded.

The other experiments were all made with freshly-caught flies from uninhabited places on the Lake-shore. The Lake-shore, as stated above, had been cleared of its inhabitants in December, 1907, and had, therefore, been deserted for nearly a year when these experiments began. It was anticipated that the flies would be found non-infective, as, in the absence of Sleeping Sickness cases, it was difficult to understand where they could obtain the necessary trypanosomes, and at this time the long period of infectivity of the fly was unknown. The following experiments give the result:—

Experiment 214.—Monkey.

To ascertain if *Glossina palpalis*, caught on the Lake-shore, where there are no natives, are capable of giving rise to Sleeping Sickness in healthy monkeys.

Date.	No. of Flies.		Trypano- somes.	Malaria.	Date.	No. of Flies.		Trypano- somes.	Malaria.
	Put on.	Fed.				Put on.	Fed.		
1908.					1909.				
Nov. 23	21	10			Jan. 4	—	—	—	+
" 24	25	20			" 9	—	—	—	+
" 25	50	26	—	+	" 15	—	—	—	—
" 26	30	17	—	+	" 25	43	24	—	—
" 27	12	8			" 26	35	29	—	+
" 28	96	23	—	+	" 28	—	—	—	+
" 30	125	41	—	+	Feb. 2	100	65	—	+
Dec. 1	150	60	—	+	" 3	105	105	—	—
" 2	—	—	—	+	" 4	100	90	—	—
" 3	—	—	—	+	" 5	—	—	—	+
" 4	—	—	—	+	" 6	100	85	—	—
" 5	60	23	—	+	" 8	100	82	—	—
" 7	47	26	—	+	" 9	200	165	—	—
" 12	60	49	—	+	" 10	200	146	—	+
" 14	83	37	—	—	" 15	200	135	—	+
" 15	78	32	—	+	" 16	200	120	—	—
" 17	14	6	—	—	" 17	170	126	—	—
" 18	—	—	—	+	" 18	200	134	—	—
" 23	—	—	—	+	" 19	200	110	—	+
" 28	80	35	—	+	" 20	200	124	—	—
" 30	70	32	—	+	" 22	130	98	—	—
					" 23	200	140	—	—
					" 24	200	142	—	—
					" 25	200	135	—	—
					" 26	—	—	—	+
					Mar. 1	—	—	+	+

Remarks.—2,500 flies were fed on this monkey for 98 days before a positive result was obtained.

Experiment 571.—Monkey.

Date.	No. of Flies.		Trypano- somes.	Malaria.	Date.	No. of Flies.		Trypano- somes.	Malaria.
	Put on.	Fed.				Put on.	Fed.		
1909.					1909.				
Mar. 2	200	152			Mar. 15	200	152		
" 3	200	156			" 16	100	78		
" 4	100	78			" 17	100	74		
" 6	150	110			" 18	100	58	—	+
" 9	200	120	—	—	" 20	200	112		
" 10	200	110			" 22	—	—	+	+
" 11	200	124							

Remarks.—Result positive. Infection probably took place on March 15. This means that 1,002 flies fed on this monkey before infection took place.

Experiment 612.—Monkey.

Date.	No. of Flies.		Trypano- somes.	Malaria.	Date.	No. of Flies.		Trypano- somes.	Malaria.
	Put on.	Fed.				Put on.	Fed.		
1909.					1909.				
Mar. 25	340	185			Mar. 29	100	76		
" 26	250	124			" 30	200	115	—	+
" 27	200	115			April 6	—	—	+	+

Remarks.—Result positive. Infection probably March 30; 615 flies.

Experiment 674.—Monkey.

Date.	No. of Flies.		Trypano- somes.	Malaria.	Date.	No. of Flies.		Trypano- somes.	Malaria.
	Put on.	Fed.				Put on.	Fed.		
1909.					1909.				
April 8	250	160			April 23	270	180		
" 9	500	240			" 26	200	160	—	—
" 10	500	220			" 28	400	240		
" 12	500	245	—	+	" 30	400	160		
" 15	500	340			May 1	500	290		
" 19	—	—	—	—	" 3	—	—	—	+
" 20	250	180			" 7	—	—	++	+
" 22	300	190	—	—					

Remarks.—Result positive. Infection April 30; 2,315 flies.

Experiment 758.--Monkey.

Date.	No. of Flies.		Trypano- somes.	Malaria.	Date.	No. of Flies.		Trypano- somes.	Malaria.
	Put on.	Fed.				Put on.	Fed.		
1909. May 8	270	210			1909. May 22	—	—	—	+
" 11	250	170			" 28	200	130	—	+
" 14	200	120			June 2	—	—	—	+
" 17	—	—	—	+	" 7	—	—	+	+

Remarks.—Result positive. Infection May 28; 630 flies.

Experiment 976.—Monkey.

Date.	No. of Flies.		Trypano- somes.	Malaria.	Date.	No. of Flies.		Trypano- somes.	Malaria.
	Put on.	Fed.				Put on.	Fed.		
1909. June 9	800	260			1909. June 18	200	90	—	+
" 10	450	180			" 20	520	230	—	+
" 17	550	190			" 21	—	—	++	+

Remarks.—Result positive. Infection June 10; 440 flies.

Experiment 1117.—Monkey.

Date.	No. of Flies.		Trypano- somes.	Malaria.	Date.	No. of Flies.		Trypano- somes.	Malaria.
	Put on.	Fed.				Put on.	Fed.		
1909 June 24	200	120			1909. June 30	7	4		
" 25	300	160			July 1	—	—	—	+
" 26	150	80			" 3	500	130		
" 28	380	165			" 5	500	220	+	+
" 29	500	210							

Remarks.—Result positive. Infection June 28; 525 flies.

Experiment 1276.—Monkey.

Date.	No. of Flies.		Trypano- somes.	Malaria.	Date.	No. of Flies.		Trypano- somes.	Malaria.
	Put on.	Fed.				Put on.	Fed.		
1909. July 9	110	70			1909. July 19	—	—	—	+
" 12	500	230			" 20	300	180		
" 15	—	—	—	+	" 22	—	—	+	+

Remarks.—Result positive. Infection July 12; 300 flies.

Experiment 1462.—Ox.

Date.	No. of Flies.		Trypano- somes.	Malaria.	Date.	No. of Flies.		Trypano- somes.	Malaria.
	Put on.	Fed.				Put on.	Fed.		
1909. Aug. 16	120	75	—		1909. Aug. 20	170	80		
" 17	410	250			" 24	350	120	—	
" 19	320	180	—		" 26	—	—	+	

Remarks.—Result positive. Infection August 19; 505 flies.

Experiment 1465.—Ox.

Date.	No. of Flies.		Trypano- somes.	Malaria.	Date.	No. of Flies.		Trypano- somes.	Malaria.
	Put on.	Fed.				Put on.	Fed.		
1909. Aug. 27	150	90			1909. Sept. 7	—	—	—	
" 28	60	35			" 9	30	19		
Sept. 4	230	170			" 10	—	—	++	

Remarks.—Result positive. Infection September 4; 295 flies.

Experiment 982.—Ox.

Date.	No. of Flies.		Trypano- somes.	Malaria.	Date.	No. of Flies.		Trypano- somes.	Malaria.
	Put on.	Fed.				Put on.	Fed.		
1909.					1909.				
Sept. 11	45	36			Sept. 20	—	—	—	
" 12	65	50			" 21	115	85	—	
" 14	110	75			" 22	180	145		
" 15	125	95			" 23	410	380		
" 16	420	160	—		" 24	300	240	—	
" 19	55	40			" 27	370	230	++	

Remarks.—Result positive. Infection, September 19; 456 flies.

The following table summarises these results:—

Experiment.	Place.	No. of Flies. fed.	No. of Days before Infection took place.	Result.	Percentage of Infected Flies.*
52	Kibanga	91	—	—	—
214	Uninhabited Lake- shore.	2500	98	+	0·04
571	" "	1002	20	+	0·10
612	" "	615	12	+	0·16
674	" "	2315	29	+	0·04
758	" "	630	30	+	0·16
976	" "	440	12	+	0·23
1117	" "	525	11	+	0·19
1276	" "	300	13	+	0·33
1462	" "	505	10	+	0·19
1465	" "	295	14	+	0·34
982	" "	456	16	+	0·22

* This is calculated on the assumption that there is only one infected fly in each batch of flies used in an experiment.

It must therefore be concluded that the Glossina palpalis on the uninhabited shores of Victoria Nyanza can retain their infectivity for a period of at least two years after the native population has been removed. How much longer they will remain infective it is impossible to say, but it is obvious that these experiments should be continued, in order to answer this important question.

With the facts at our disposal it is not possible to account for this continued infectivity. It may be due to the duration of the life of these flies being more than two years—that flies which became infected before the natives left are still alive. Or, it is possible that the flies have lately fed on natives suffering from Sleeping Sickness, who have been passing in canoes from the islands to the mainland, or on natives who still frequent the

Lake-shore in spite of the prohibition. Thirdly, it might be explained, if any of our canoe-men or fly-boys had trypanosomes in their blood. Or, lastly, it is possible that the mammals and birds along the Lake-shore have become infected, and so act as a reservoir of the disease.

To these speculations it may be answered that it is not at all likely that these flies have the opportunity of becoming infected from passing canoes, which during the last two years have been few and far between, or to natives still frequenting the Lake-shore. Our canoe-men and fly-boys have been kept under careful supervision during the whole of the time, their blood constantly examined, and once a month blood from each of them injected into a healthy monkey. There remain, then, the two theories—long duration of life of the fly, and a local reservoir. The former cannot at present be answered, and there is no experimental proof of the latter, since the injection of the blood of the Lake-shore birds and mammals into susceptible animals has always, up to the present, given negative results.

[Reprinted from the PROCEEDINGS OF THE ROYAL SOCIETY,
B. Vol. 82.]

36. GLOSSINA PALPALIS AS A CARRIER OF TRYPANOSOMA VIVAX IN UGANDA.

By Colonel Sir DAVID BRUCE, C.B., F.R.S., Army Medical Service; Captains A. E. HAMERTON, D.S.O., and H. R. BATEMAN, Royal Army Medical Corps; and Captain F. P. MACKIE, Indian Medical Service. (Sleeping Sickness Commission of the Royal Society, 1908-09.)

(Received November 27,—Read December 9, 1909.)

One of the important trypanosome diseases of cattle in Uganda is that caused by *Trypanosoma vivax* (Ziemann). This species of trypanosome appears to be widely distributed in Central Africa. It has been reported from Senegal, the Sudan and Erythrea in the North, to Rhodesia in the South. It is fairly easily recognised on account of its extreme activity during life, its characteristic shape in stained specimens, and the fact that it only affects cattle, goats, and sheep; while monkeys, dogs, rabbits, guinea-pigs, rats, and mice are refractory. Its carriers have usually been reported as tabanus and stomoxys.

This short note is written to place on record that fact, that in Uganda the tsetse flies, *Glossina palpalis*, which are found in large numbers on the Lake-shore, are infected, not only by *Trypanosoma gambiense*, the cause of sleeping sickness, but also by *Trypanosoma vivax*. The first experiment which showed that

these tsetse flies are infected with the latter trypanosome was the following:—

Experiment 1318.—Calf.

To ascertain if oxen will become infected by trypanosomes if allowed to feed in the “fly area.”

July 12, 1909. A healthy calf was taken down to the Lake-shore at Kibanga and ferried across the bay to Nsonga, where tsetse flies are numerous. The flies were observed to feed on it in numbers. It was then brought back to Kibanga. In future this calf will be taken out every day by the fly-boys to different parts of the Lake-shore, where it will graze while the boys are catching tsetse flies.

August 8. Returned from Lake-shore to Mpumu.

August 11. *Trypanosoma vivax* present in the blood of this calf.

Remarks.—If the incubation period of this disease is assumed to be eight days, then this calf remained 19 days at the Lake-shore before it became infected. The proof that the trypanosome found in this calf's blood was *Trypanosoma vivax* and not *Trypanosoma gambiense* was the shape and appearance of the parasite, the fact that the calf's blood injected under the skin of two monkeys gave negative results, and, lastly, that 50 laboratory-bred flies fed on this calf afterwards infected a goat with *Trypanosoma vivax*.

Experiment 431.—Cow. (Mother of Calf, 1318.)

July 12, 1909. This cow accompanied her calf to Kibanga, and remained with it during the experiment.

August 8. Returned to Mpumu.

August 19. *Trypanosoma vivax* discovered in blood.

The following table shows the dates of examination:—

Date.				Parasites in Blood.	
				Piroplasma.	Trypanosoma.
1909.					
January	9	—	—
"	20	—	—
"	21	—	—
"	28	—	—
February	2	—	—
"	9	—	—
"	26	—	—
August	9	—	—
"	11	—	—
"	19	—	+

Remarks.—It is possible that this cow became infected from her calf, but it is more probable that she became infected in the same way and about the same time as her calf.

The remaining experiments were carried out by bringing freshly-caught *Glossina palpalis* from the Lake-shore to the laboratory at Mpumu and placing them on healthy oxen.

Experiment 1462.—Bull.

To ascertain if freshly-caught *Glossina palpalis*, fed on healthy cattle, will give rise to any trypanosome disease.

Date.			Flies.		Result.	
			Put on.	Fed.	<i>T. gambiense.</i>	<i>T. vivax.</i>
1909.						
August	16	...	120	75	—	—
"	17	...	410	250		
"	19	...	320	180	—	—
"	20	...	170	80		
"	24	...	350	120	—	—
"	26	...			+	—
September	1	...			—	+
"	2	...			—	+
"	3	...			—	+
"	4	...			—	+
"	6	...			+	+
"	7	...			+	+
"	8	...			+	+
"	9	...			—	+

Remarks.—Both *Trypanosoma gambiense* and *Trypanosoma vivax* appeared in the blood of this bull.

Experiment 445.—Bull.

Date.			Flies.		Result. <i>Trypanosoma</i> <i>vivax.</i>
			Put on.	Fed.	
1909.					
September	28	...	470	220	
"	29	...	160	95	
"	30	...	65	45	—
October	1	...	300	180	
"	2	...	400	280	
"	4	...	500	300	—
"	5	...	190	85	
"	7	...	250	170	—
"	8	...	300	165	
"	11	...	100	70	—
"	15	...	450	360	—
"	16	...	470	350	
"	18	...	—	—	+
"	19	...	—	—	++

Remarks.—*Trypanosoma vivax* only appeared in the blood of this bull.

Experiment 1465.—Bull.

Date.				Flies.		Result.	
				Put on.	Fed.	<i>T. gambiense.</i>	<i>T. vivax.</i>
1909.							
August	27	150	90	—	—
"	28	60	35	—	—
September	4	230	170	—	—
"	7	—	—	—	—
"	9	30	19	—	—
"	10	—	—	—	+
"	11	—	—	+	—

Remarks.—Both *Trypanosoma gambiense* and *Trypanosoma vivax* appeared in the blood of this bull.

Experiment 982.—Bull.

Date.				Flies.		Result.	
				Put on.	Fed.	<i>T. gambiense.</i>	<i>T. vivax.</i>
1909.							
September	11	45	36		
"	12	65	50		
"	14	110	75		
"	15	125	95		
"	16	420	160	—	—
"	19	55	40		
"	20	—	—	—	—
"	21	115	85	—	—
"	22	180	145		
"	23	410	380		
"	24	300	240	—	—
"	25	—	—	—	—
"	27	370	230	+	—
October	14	—	—	—	+

Remarks.—Both *Trypanosoma gambiense* and *Trypanosoma vivax* appeared in the blood of this bull.

Conclusions.

1. The *Glossina palpalis* on the shores of Victoria Nyanza are infected, not only by *Trypanosoma gambiense*, but also by *Trypanosoma vivax*.

2. What the reservoir of the virus of *Trypanosoma vivax* is, is unknown, but the buffalo, waterbuck, and other antelope which live on the Lake-shore should be examined.

37. ON THE ACTION OF ANTIMONY COMPOUNDS IN
 TRYPANOSOMIASIS IN RATS: BEING A REPORT
 TO A SUB-COMMITTEE OF THE TROPICAL
 DISEASES COMMITTEE OF THE ROYAL SOCIETY.

By JOHN D. THOMSON, M.B., C.M., and ARTHUR R. CUSHNY,
 M.D., F.R.S.

(Received November 23, 1909,—Read January 20, 1910.)

The near chemical and pharmacological relation of arsenic and antimony suggested naturally the use of the latter in a disease in which the former has proved of value; but the irritant action of the ordinary antimony salts seemed to preclude their use by hypodermic injection. After repeated attempts to form organic compounds of antimony analogous to atoxyl, one of us (C.) submitted to Plimmer and Thomson, for experimental trial, a compound of glycine and antimony, and their results with it showed that antimony possesses trypanocidal properties. This antimony compound proved difficult to make and unstable, however, and these observers substituted for it tartar emetic; the results were satisfactory, and the following investigation was undertaken with the object of determining the limits of usefulness of other antimony compounds in these diseases. The experiments were made on rats infected with a strain of Nagana (*T. brucei*) obtained by the kindness of Sir J. McFadyean. This strain was fatal to rats within six days after inoculation, or within three days after trypanosomes appeared in the blood. The inoculation and treatment were carried out at the Lister Institute of Preventive Medicine.

In the use of the heavy metals it is generally recognised that the more readily dissociated compounds are liable to cause more local irritation than others, and where the local action is to be avoided, attempts are made to use compounds which are less immediately dissociated and pass into the general tissues in their original form, there to free the metallic ion compound which is necessary for the desired effect.

An example of this is offered in the substitution of atoxyl for the older arsenic preparations in the treatment of trypanosomiasis, for there is no question that the atoxyl owes its activity to the simpler compounds formed from it in the tissues. It is possible that, in addition to avoiding local irritation, such compounds as atoxyl may penetrate into cells which are not permeable by ordinary arsenic salts, and that the latter may in this way be liberated in cells to which they would not otherwise have had access.

With this in mind it seemed desirable to test the action of compounds in which antimony is more firmly combined than the ordinary salts, but very few organic combinations are available, and we have succeeded in obtaining only two such for investigation. Of these the first was tetraethylstibonium iodide ($(C_2H_5)_4SbI$), which was injected into seven Nagana rats in

quantities up to 20 milligrammes, but had no effect whatever on the parasites, the injected animals dying at the usual time, and the blood being found to be swarming with trypanosomes. The other, diphenylstibinchloride ($(\text{C}_6\text{H}_5)_2\text{SbCl}_3, \text{H}_2\text{O}$), was kindly put at our disposal by Professor A. Michaelis, of Rostock, but proved quite devoid of action in quantities of 4 c.c. of a saturated solution in sodium carbonate, in which it is more soluble than in water. These compounds appear non-irritant, but the antimony is probably not freed in the tissues, the first compound in particular resembling the ammonium salts, which pass through the animal body without freeing nitrogen.

These compounds proving valueless for our purpose, it was determined to find in what form the antimony ion had to be liberated to be effective, and a number of compounds commercially obtainable were tested. Of these the potassium metantimoniate (SbO_2OK), injected in quantities up to 30 milligrammes, scarcely affected the trypanosomes in the blood; doses above 30 milligrammes were followed by the disappearance of the parasites from the circulation, but the rats became very ill and died within a few days, and *post mortem* enteritis and nephritis were found to have been developed. A preparation of antimony oxide (Sb_2O_3), stated to be in colloidal form, was obtained from Kalle and Co., but proved extremely irritating, and had a very low efficiency. The preparation contained 4.5 per cent. of antimony oxide only, and in quantities corresponding to 4 milligrammes of the oxide had little, if any, effect in reducing the number of trypanosomes in the blood; 8 milligrammes caused their disappearance, but they recurred on the fourth day.

In the former of these preparations antimony is presented in pentavalent, in the latter in trivalent, form, and both are equally inefficient, while in the forms in which it is presented in combination with organic acids it is also in trivalent form, but has been shown to have a high degree of activity. It is possible that, given in the colloid form, it is deposited locally and fails to reach the trypanosomes. This would also explain the intense local action, which was more marked from this than from any other preparation.

A glyceride of antimony, analogous to boroglyceride, was formed by heating glycerine with the oxide, and proved fairly effective in destroying the trypanosomes in the rats, but it was very irritant and caused hæmoglobinuria, and the solution in glycerine tended to deposit the oxide when diluted.

A few experiments were made with Schlippe's salt, sodium sulphantimonate ($(\text{NaS})_3\text{SbS}$); it destroyed the trypanosomes in the rat very satisfactorily (*see* Table I.), but induced very considerable local reaction, and therefore appears to be precluded from use in therapeutics. This result agrees with that obtained by Broden and Rodhain* in man.

* 'Arch. f. Schiffs- u. Tropenhygiene,' vol. 12, No. 14, 1908.

Table I.—Summary of Results of Treatment with Schlippe's Salt.

I.	II.	III.	IV.
Number of Rats treated.	Number of Rats that died without recurrence, but before any deduction could be made.	Number of Rats surviving over one month after cessation of treatment without recurrence.	Number of Rats in which recurrence occurred.
20	6	3	11

Of the rats included in Column III.: One survived 39 days, one 33 days, and one 76 days. The cause of death did not seem to be the disease or its treatment.

Of the rats included in Column IV.: Recurrence took place in 10, 21, 9, 10, 10, 13, 7, 13, 16, and 14 days, and all died within two weeks of the cessation of treatment from the recurrence (or from the last recurrence, for many had more than one recurrence), with the exception of one which was alive and well 244 days after cessation of treatment of the recurrence—the latter by another drug (sodium antimonyl tartrate).

In Schlippe's salt and in the glyceride, antimony is pentavalent, and these were efficient trypanocides, especially the former, while the metantimoniate, where antimony is also pentavalent, possessed a low efficiency.

The sulphantimoniate differs from the metantimoniate in its great instability, and it seems probable that the marked local reaction arising from it is due in great part to its being decomposed at the point of injection with the deposit of the insoluble antimony sulphide Sb_2S_3 , which produces a slow, lasting reaction. Enough reaches the general tissues, however, to react with the parasites, and here its instability, permitting of its forming new compounds, renders it peculiarly active. The metantimoniate, on the other hand, is much more stable, and probably fails to be reduced to the trivalent form.

The greater number of our experiments were done with the combinations of antimony with the organic acids corresponding to the ordinary tartar emetic. Among these the best combinations were found to be those with oxyacids of the fatty series, those of the aromatic series proving much less soluble. Among the salts examined were the lactate, citrate, malate, and mucate, the results of which were compared with those obtained by the tartrate.

They were formed by boiling antimony oxide with the acids, and subsequently neutralising with sodium hydrate, or sometimes by forming the acid sodium salt, and boiling it with freshly prepared antimony oxide. The mucate, which was investigated with the idea that its multiple hydroxyl groups might prove to have special powers of retaining antimony in solution, may be dismissed, as, though powerfully trypanocidal, it induced very great local irritation. The citrate seemed to be inferior to the malates and tartrates, which were approximately equal in value.

Table II.—Summary of Results of Treatment with Sodium Antimonyl Malate.

I.	II.	III.	IV.
Number of Rats treated.	Number of Rats that died without recurrence, but before any deduction could be made.	Number of Rats surviving one month after cessation of treatment without recurrence.	Number of Rats in which there was recurrence.
23	9	5	9

Of the rats included in Column III.: One survived 241 days; one 113 days; one 115 days; one 66 days; and one was alive and well 235 days after cessation of treatment.

Of the rats included in Column IV.: Recurrence took place in 12, 11, 7, 17, 5, 11, 9, 36, and 10 days, and all died within two weeks of cessation of treatment of recurrence (or of the last recurrence), except one which lived 231 days after cessation of treatment of the recurrence by another drug (Schlippe's salt).

Among the tartrates and malates, the sodium and potassium salts were equally efficient trypanocides, and there was no appreciable difference in their local effects, but the substitution of an alkyl radical for the potassium or sodium of the salt seemed to be attended with some advantage. Solutions of ethylantimonyl tartrate were kindly prepared for us by Professor Collie by heating freshly precipitated antimony oxide with ethyl tartrate, to about 150° C. in sealed tubes. The solutions are distinctly acid, but can be neutralised or rendered slightly alkaline with ammonia, and can be sterilised by boiling without any cloudiness resulting. It is a very efficient trypanocide and causes no local irritation in the rat. After the injection of 1 c.c. of a 0.2-per-cent. solution* into rats of 100 to 200 grammes weight, trypanosomes, though previously numerous, entirely disappear from the peripheral blood within one to two hours. Estimated by the amount of antimony present in the solutions, the ethyl is more powerfully trypanocidal than the sodium salt, which may suggest either that less is deposited at the point of application, or that it reaches the trypanosomes in a more readily penetrating form.

Though more poisonous to the rat than sodium antimonyl tartrate, the *range* of dose, or the difference between the effective trypanocidal dose and the lethal dose, is not less than that of the other antimony preparations. The optimum dose may be found to correspond to Browning's therapeutic dose, viz.: two-thirds of the maximum dose that average animals tolerate.

From our own work, and that of others, we think that sufficient data have been obtained to indicate some points which must be

* The strength of the solution was ascertained by estimation of the antimony

taken into consideration in attempting further advance in the treatment of trypanosomiasis:—

(1) As regards the compound it must be non-irritant and capable of remaining in perfect solution at the temperature and alkalinity of the tissues.

(2) It must act quickly on the trypanosomes, for otherwise these parasites seem to acquire a tolerance to it. It is possible that some drugs may require to be altered in the tissues before they begin to affect the parasites; but with this proviso, we suggest, as a working rule, that no drug which, given in full therapeutic dose, does not destroy the trypanosomes in the blood within two hours is likely to prove an advance on remedies already in use.

(3) When the trypanosomes have been expelled from the blood by a single full therapeutic dose, there must be no recurrence in the majority of cases within some fixed time, which will vary with the particular host, and the species and strain of trypanosome in use; the length of this period must be determined by each investigator by reference to some of the known trypanocides. In our experiments it proved waste of time to persevere with any drug whose administration in a single full dose was followed by a recurrence in the majority of cases within a week. The longer the time during which there is no recurrence in the majority of animals treated the more promising is the outlook for the drug under trial. But the non-recurrence in a single individual is of comparatively small importance.

In our experiments the majority of the rats that survived the injection for three weeks showed recurrence within that time, except when ethyl antimonyl tartrate was employed, when the results were slightly more favourable.

In the recent report* from Uganda, the conclusion is drawn that the medicinal treatment pursued up to that time had proved of little lasting benefit in the great majority of even the early cases of sleeping sickness. From this it seems a fair inference that remedies which suffice to change an acute trypanosomiasis into a more chronic form may ameliorate symptoms, but do not necessarily greatly prolong the natural course of a chronic infection such as sleeping sickness. In seeking for a remedy for the chronic condition, by experiments with acute infections, nothing short of an immediate and complete disinfection should be the object, and it is with this view that we venture to suggest the foregoing considerations.

Applying these principles to the ethyl antimony compound, it appears to comply with the first fairly satisfactorily. It expelled the trypanosomes from the blood within two hours. As regards recurrence after a single full dose, of 13 rats inoculated, 6 showed a recurrence, on the 14th, 16th, 16th, 22nd, 26th, and 29th day. There was no recurrence in the 7 others.

* Quarterly Report on the Progress of Segregation Camps and Medical Treatment of Sleeping Sickness in Uganda (Quarter December 1, 1907, to February 29, 1908).

Table III.—Summary of Results of Treatment with Ethylantimonyl Tartrate.

I.	II.	III.	IV.
Number of Rats treated.	Number of Rats that died without recurrence, but before any deduction could be made.	Number of Rats surviving over a month after treatment without recurrence.	Number of Rats in which there was recurrence.
13	0	7	6

Of the rats included in Column III., one died of pneumonia on the 84th day, and five of the others from exposure to cold between the 135th and 165th day, leaving one survivor after 260 days.

Of the rats in Column IV., recurrence took place after 14, 16, 16, 22, 26, and 29 days respectively.

No other drug has given such favourable results in our experiments, but we recognise that it will be necessary to test it against other species and strains and in different hosts before any general statement as to its usefulness can be made.

We have also treated some rats with a solution combining the best of the arsenical and antimonial trypanocides at present known to us, viz., ethylantimonyl tartrate and atoxyl. Twelve rats were inoculated with the Nagana strain, and on the third day after, when a fair number of trypanosomes were present in the blood, they received a single injection of 0.75 c.c. of a solution containing 2 per cent. of atoxyl dissolved in 0.2 per cent. of ethylantimonyl tartrate.

Table IV.—Summary of Results of Treatment with Atoxyl + Ethylantimonyl Tartrate.

I.	II.	III.	IV.
Number of Rats treated.	Number of Rats that died without recurrence, but before any deduction could be made.	Number of Rats surviving over a month after treatment without recurrence.	Number of cases of recurrence.
12	2	8	2

Of the rats included under Column III., two died in 31, one each in 39, 43, 56, 89 days, and two survived after 260 days. Thus, while the number of recurrences was fewer than from the antimony alone, the combination of the two drugs seemed to tend to be toxic. This was more obvious in a series of 19 rats treated with a single injection of 0.75 c.c. of 3-per-cent. atoxyl in 0.3-per-cent. ethylantimonyl tartrate solution. Of these, 11 died within 24 hours of the injection, and as the blood was free from trypanosomes, they evidently succumbed to the treatment.

Table V.—Summary of Results of Treatment with Larger Doses of Atoxyl and Antimony.

I.	II.	III.	IV.
Number of Rats treated.	Number of Rats that died without recurrence, but too soon for any deduction.	Number surviving over a month without recurrence.	Number of cases of recurrence.
19	16	2	1

Of the two rats included in Column III., one died on the 113th day, and one survived after 225 days. The recurrence noted in Column IV. was noted on the 25th day. One of those in Column II. had trypanosomes in the blood the day after treatment and died that day.

The results of the combined medication were thus scarcely superior to those of the ethylantimonyl tartrate alone, for though there were fewer recurrences when atoxyl was added, the mortality from poisoning was higher, so that only two survived for two months as against six of those treated with antimony alone. It is possible that by a more accurate adjustment of the two drugs the advantages of diminished recurrence and low toxicity might be combined.

38. REPORT ON A COLLECTION OF BLOOD-PARASITES MADE BY THE SLEEPING SICKNESS COMMISSION, 1908-09, IN UGANDA.

By E. A. MINCHIN, M.A., Professor of Protozoology in the University of London.

(Plates 7, 8, 9.)

The following report deals with a collection of slides sent home by Sir David Bruce from Uganda, and entrusted to me for further investigation by the Royal Society. The whole collection consisted of 27 slides bearing blood-smears taken from amphibia, reptiles, and birds (no mammals), all stained by the Romanowsky method, some with Giemsa's stain, others with Leishman's. I have no information as to the method by which the blood was fixed, but the films seem to have been prepared by the ordinary method of drying in air, followed by fixation with absolute alcohol or methyl-alcohol. In some cases the smears are covered, in others not.

With the slides were a number of coloured drawings by Lady Bruce of the parasites in the smears. Some of these drawings are reproduced here, together with a certain number drawn from the preparations by my assistant, Miss Rhodes. With regard to these drawings I wish to make one observation. All Lady

Bruce's drawings were stated to have been executed at a magnification of 2,000 diameters, a standard magnification which I always employ for blood-parasites of this kind, unless they are excessively minute. When, however, Miss Rhodes drew parasites from these slides at a magnification of 2,000, they came out appreciably larger than Lady Bruce's drawings of the same parasites. I then checked the magnification of Miss Rhodes's drawings carefully by the method of drawing the divisions of the scale of a stage-micrometer, using the same camera lucida, eyepieces, objectives, and microscope, with the same length of tube, in short the same arrangements in every detail that Miss Rhodes had used in making her drawings; and I found that the magnification was as accurately 2,000 as it was possible to make it. In order to compare the magnifications of the two sets of drawings, Miss Rhodes drew with the camera lucida the outlines of some red blood-corpuscles of the small toad (*see* below), to compare with drawings of corpuscles from the same slide made by Lady Bruce. It was then found that the corpuscles drawn by Miss Rhodes at a magnification of 2,000 averaged 35 mm. in length, while those drawn by Lady Bruce averaged 29 mm. in length. From these measurements I calculate that Lady Bruce's drawings are really magnified between 1,600 and 1,700 diameters.

The simplest method of dealing with a collection of material of this kind is first to enumerate the hosts in systematic order, stating briefly the forms of parasites that occur in each, and then to deal with points of interest presented by the various forms of parasites. I may state at once that no new or unknown types of blood-parasites have been discovered in these slides, but nevertheless some of the observations are well worth recording; perhaps the most interesting result of this investigation is the comparison of Halteridia from a number of different species of birds, which has not, to my knowledge, been undertaken before. It will be seen that the Halteridia differ from one another in structural characters in a marked manner and to an extent which, I must confess, was a surprise to me.

I. THE HOSTS AND THEIR PARASITES.

Amphibia.

This class of vertebrates is represented by one slide and a drawing, labelled "Small toad from Kibanga, 28.11.08." The slide is, however, a very interesting one, since the smear contains two forms of trypanosomes fairly abundantly. One of these trypanosomes (pl. 9, figs. 61-63) is very large and similar in every way to *Trypanosoma mega*, Dutton and Todd (1903, pp. 51-53, pl. II., fig. 4), which was discovered by these investigators in "small frogs caught in a marsh at McCarthy Island." The other trypanosome is much smaller (pl. 9, fig. 64) and different in its characters; it is also generally not so well preserved on this slide as the large form, and it is difficult to find good specimens of it to draw. In all the trypanosomes in this

smear both the trophonucleus and the flagellum are faintly stained; the free flagellum can only be seen with critical illumination.

As regards the large type of trypanosome, its chief characters, in addition to its large size, are as follows: the trophonucleus is placed slightly behind the middle of the body, and appears in the Romanowsky-stained preparations as a large oval space, placed transversely and stretching across the whole width of the body, usually quite clear, but sometimes showing a few grains tinged a faint red (pl. 9, fig. 63). The surface of the pre-nuclear region of the body shows very distinct longitudinal striations in the form of dark streaks, stained bluish or purplish, alternating with light streaks, or perhaps more correctly spaces, which are broken up into a succession of alveoli by thinner transverse dark streaks connecting the thicker longitudinal streaks already mentioned. This system of striations is generally interpreted as a system of myonemes or contractile fibrillæ, the light interspaces being regarded as the contractile elements themselves; but the preparations I have before me suggest strongly that the dark streaks should be identified as the actual contractile elements, if anything. This question cannot, however, be decided by a stain so unreliable for finer details of structure as the Romanowsky combination, and no other preparations are available. The striations are continued over the nucleus into the hinder part of the body, where, however, they become less distinct and obscured by coarse granulations.

It is interesting to note that in the pre-nuclear region the striations sometimes run nearly parallel on the two surfaces of the body, and in other cases cross each other, those seen at the higher focus being often nearly at right angles to those at the lower focus, indicating clearly that in the latter case the body has a spiral twist more or less pronounced (pl. 9, fig. 62). These appearances were noticed also by Dutton and Todd.

The kinetonucleus is not very large, generally oval in outline, and stains deeply; it is always close behind the trophonucleus, and there is a long postnuclear region of the body, sometimes greatly drawn out and attenuated. The flagellum arises from close beside the kinetonucleus and runs along the edge of a fairly deep undulating membrane, finally ending as a free flagellum of moderate length. The undulating membrane shows about a dozen pleats, deeper posteriorly and shallower anteriorly. The course taken by the undulating membrane is very instructive when compared with the arrangement of the myoneme-striations (pl. 9, figs. 61, 62). In those specimens in which the striations are straight and parallel on the two sides of the body (fig. 61), the body lies in the form of a C, and the undulating membrane runs along the convex side of the curve. When, however, the myoneme-striations cross each other on the two surfaces of the body (pl. 9, fig. 62), the body itself has one or more S-like curves, and the undulating membrane, keeping always to the convex side of a curve, crosses over or under the body at each spot where the curvature changes. In all cases alike it can be seen that the undulating membrane is parallel to those

myoneme-striations which are nearest to it at its line of attachment to the surface of the body, and that the differences in the course of the undulating membrane in different specimens are due simply to the degree of spiral twisting in the body indicated, as already stated, by the myoneme-striations; possibly, indeed, caused by the contractility of the myonemes themselves.

The other type of trypanosome on this slide, besides being much smaller (pl. 9, fig. 64), has a moderately-sized tropho-nucleus placed in the posterior half of the body and far removed from the kinetonucleus, which is relatively close to the posterior termination of the body, so that the post-nuclear portion of the body is short. The flagellum arises close to the kinetonucleus and the undulating membrane is not greatly pleated. The body does not show distinct myoneme-striations, but the cytoplasm presents the appearance of vacuoles which sometimes are arranged in longitudinal series, an arrangement perhaps due to the existence of myoneme-bands.

The question at once suggests itself, whether these two forms of trypanosome belong to the same or to different species. With regard to the large forms, trypanosomes of this type have been described by several observers from African frogs since they were first discovered by Dutton and Todd in 1903; for instance by Dutton, Todd, and Tobey (1907) and by Rodhain (1908), all of whom consider that both the *mega*-type and the other types of form observed in frogs are all simply developmental variations of the common *T. rotatorium*, and Laveran and Mesnil also incline to this view in their well-known work on trypanosomes (1907, pp. 465-473). It would hardly be profitable to discuss this question on the evidence presented by a single slide. I may remark merely that if all the various forms described from frogs belong to one species, then the two forms occurring on Sir David Bruce's slide may well be two forms of the same species also. On the other hand the frequent occurrence, to judge from the literature, of *Trypanosoma mega* from African frogs, and the fact that it has not been recorded, so far as I am aware, from European frogs, seems to me to indicate that *T. mega* is a species distinct at all events from the European *T. rotatorium*.

Reptilia.

(1) *Lacertilia*.—The collection contains one slide labelled simply "lizard" without any further indication as to the species; some drawings have been made from it by Lady Bruce (pl. 7, figs. 20-23), which show an infection with an intra-corpuseular pigmented hæmamœba of the type of the *Hæmamœba metschnikovi* described by Simond from an Indian tortoise. Such forms are now known from various reptiles and have been placed by Willey in a separate genus *Hæmocystidium*, but the majority of writers include them in the comprehensive genus *Plasmodium* (*Hæmamœba*). In the present instance large free forms are also seen (pl. 7, fig. 20), which have evidently been liberated from the corpuscles, either by their own efforts, or it may be by rupture of the corpuscle in making the smear. The film is unfortunately a defective one; in many places the corpuscles are

run together, and only their nuclei are distinguishable; in other places there is much precipitate of stain. A great many of the corpuscles present the appearance of young *Hæmocystidia* in their interior, but I am inclined to think that these appearances are caused by deposits of the stain.

(2) *Ophidia*.—There are three slides of smears of snakes' blood, each with figures drawn from them. One of the slides is labelled "Puff Adder, 15.1.09," and the accompanying drawing shows a red blood-corpuscle and a peculiar cell, and is marked "evidently a white blood-corpuscle, not a parasite," an opinion with which I entirely agree. Another slide is labelled "small snake, 13.12.08," and the corresponding drawing is marked "strange cells seen in a small snake killed on Mpumu." Having compared the drawing with the specimen, the cells in question appear to me to be also large leucocytes filled with coarse red-staining grains obscuring more or less completely a faintly stained nucleus.

The third slide is labelled "snake-blood, 3.2.09," and the drawing shows typical hæmogregarines in blood-corpuscles and is marked "same parasite in liver with a few free forms." Miss Rhodes has drawn some more figures from the film. As will be seen from the drawings (pl. 7, figs. 1-4), the hæmogregarine is a broad, more or less bean-shaped form, occurring in various stages of growth. No vermicular forms were observed, either free or coiled up in the corpuscle. The younger forms are moderately stout and do not displace the nucleus of the corpuscle; on the other hand very broad forms occur which push the nucleus to one side; there is, however, no karyolysis. Some of the hæmogregarines are extremely vacuolated. They are also in many cases very full of coarse red-stained grains, which may or may not be chromatic in nature. The nuclei of the parasites vary greatly in size and appearance, as the drawings show.

(3) *Chelonia*.—There are two slides in the collection, with drawings made from them, the one labelled "Tortoise, 10.1.09," the other "Tortoise, 15.1.09." There is no indication as to the species of tortoise, nor even whether the two smears were from the same species; since, however, the two preparations show quite similar parasites, and it is reasonable to suppose that a difference in the species of the host would have been noted, it may be inferred that both smears are taken from the same species of tortoise.

Both the tortoise-smears show hæmogregarines, very abundantly, and trypanosomes, in scanty numbers and requiring some searching to find. The hæmogregarine presents itself under a variety of forms and phases, and is found both free and intra-corpuscular.

The intra-corpuscular forms of the hæmogregarine can be classified under three types; in all cases alike the nucleus of the corpuscle is displaced, but not karyolyzed. There are first of all a small number of young forms (pl. 7, fig. 5), remarkable for the size of the nucleus, which is both relatively and absolutely larger than that of the full-grown forms, appearing as a mass

of chromatin-grains occupying nearly the whole body, and leaving only a small quantity of cytoplasm free at the two ends. Secondly, there are vermicular forms (pl. 7, figs. 6-8), curled up within the corpuscle in the characteristic manner; the nucleus in this form is generally placed near the point at which the body bends over, and is relatively small or of moderate size and usually compact; the cytoplasm stains a faint blue, as a rule, and may be quite free from granulations, but more usually contains numerous red-stained grains, sometimes aggregated in a dense clump at the thickest part of the body, where the entire cytoplasm may be stained red (pl. 7, fig. 7). The third form of parasite is broad and bean-shaped (pl. 7, figs. 10-13); the cytoplasm stains an intense blue and generally is free from red-staining grains, but the nucleus is very large, occupying the middle of the body, and appearing usually as a diffuse patch of chromatin-granules.

The free hæmogregarines (pl. 7, figs. 9, 14) found on these smears do not differ in type from the intracorpuseular forms, and they appear to me to have been set free passively, by the process of smearing out the blood on the slide, rather than by their own efforts. This conclusion is clearly indicated by the vermicular types; only in a single instance have I seen a vermicule stretched straight out, after the manner of such forms when truly free. All the other free vermicules that I have seen are curled up in just the same manner as when they are intra-corpuseular, and in many cases a delicate capsule can still be seen round them (pl. 7, fig. 9). I infer, therefore, that the free parasites in these slides have become so by rupture of the host-cell artificially.

The trypanosomes found on the slides do not call for any special remark; they are of fairly large size, and their general appearance is shown by fig. 65, pl. 9.

(4) *Crocodylia*.—The collection contains one slide, with a drawing labelled “crocodile, 3.1.09, liver.” It shows a somewhat scanty hæmogregarine-infection (pl. 7, figs. 15-19). The intra-corpuseular forms are either bean-shaped or vermicular, and in the latter case they are curled up in the characteristic manner with a distinct capsule (fig. 16). The nucleus of the corpuscle is displaced, but not karyolyzed. The free forms are for the most part similar to those found in the corpuscles, but in one case I have found a straightened-out and apparently naturally-free vermicule (fig. 19).

BIRDS.

The bulk of the collection consists of smears of bird's blood, 19 smears in all, representing 10 species of birds. On these preparations all the familiar types of avian blood-parasites are represented, namely:—

(1) The type for which Labbé's name *Halteridium* (1894) is still the most distinctive, although the name which is at present believed to be most correct, according to the rules of zoological nomenclature, is *Hæmoproteus*. I shall refer to these parasites as Halteridia, without prejudice to the vexed question of their correct designation. Their distinctive features are as follows: they are intra-corpuseular parasites of the red cells, more or less

amœboid, and containing melanin-pigment; they do not displace the nucleus of the corpuscle but grow round it, assuming the characteristic halter-like form which is expressed by Labbé's name. When the blood is drawn and cooled down without being dried, the ripe gametocytes burst their corpuscles, and the male forms "flagellate," that is to say, throw off male gametes. This habit of flagellating, and the fact that they contain melanin-pigment, distinguishes Halteridia at once from Hæmogregarines.

(2) The form which Labbé named *Proteosoma*, of which the name certified to be correct is *Plasmodium* (or *Hæmamœba*) *præcox* according to some, *P. (H.) relictum* according to others. I shall refer to it simply as the *Proteosoma*-parasite. It agrees with Halteridium in all its characteristics except one by which it is easily distinguished; namely that the parasite displaces the nucleus of the host-cell, and appears as a compact mass occupying nearly the centre of the blood-corpuscle.

(3) The *Leucocytozoon* or parasite of the white corpuscles discovered by Danilewsky (by no means to be confused with the pseudo-leucocytozoa found in some mammals, a perfectly distinct type of parasite, hæmogregarine in nature). The true avian *Leucocytozoon* is a peculiar spindle-shaped body in its full-grown form, without melanin-pigment, and with the nucleus of the host-cell attached to one side of the body of the parasite and often greatly drawn out. The adult *Leucocytozoa* show well-marked male and female types, and when the blood is drawn, the full-grown forms burst their corpuscles and round themselves off, the male forms proceeding to "flagellate" just like the two parasites already mentioned. In blood-films the attached nucleus of the host-cell generally stains deeply and is very distinct, but the nucleus of the parasite itself stains feebly and is often difficult to make out. In the preparations upon which I am reporting the nucleus of the parasite is generally not visible, or appears as an indistinct, faintly-stained patch of pinkish colour.

(4) *Trypanosomes*.—The types of avian trypanosomes are dealt with by Laveran and Mesnil in their well known treatise (1907, pp. 439-456).

In addition to the above four types of Protozoan blood-parasites, filarial worms occur in several of the preparations in this collection. Since the practice of drying blood-smears and staining them by the Romanowsky method is a very defective technique for the study of the structure of filariæ, I shall content myself with merely noting their occurrence on these slides.

I proceed now to describe the preparations of birds' blood in order:—

(1) *Guinea-fowl* (*Numida ptilorhyncha*?).*—There are seven slides of the blood of the guinea-fowl, all of different dates. The first (15.11.08) shows a very scanty infection

* The birds in this collection of slides are denoted only by popular names. Mr. R. Olgilvie Grant, of the British Museum of Natural History, has kindly furnished me with the scientific names. Those that are doubtful are marked ??, less doubtful ?.

of Halteridium. The second (27.11.08) shows Halteridium and Leucocytozoon, but the preparation is very defective and the blood in parts is hæmolyzed. The third (4.1.09) also shows a scanty infection of the same two parasites. The fourth (10.1.09) is a defective preparation; the drawing (pl. 9, fig. 72) from it represents a female Leucocytozoon which has rounded itself off, indicating that the blood was dried very slowly in making the film. The fifth (3.1.09) shows a fairly abundant infection of Halteridium, Proteosoma, and Leucocytozoon. The sixth (5.1.09) shows abundant Leucocytozoon. The seventh (15.12.08), finally, shows a very good infection with Proteosoma; there are often several parasites in a field of the immersion-lens. The parasites (pl. 8, figs. 27-32) are all in nearly the same stage, very young forms which have just entered the corpuscle and begun their growth. Sometimes also free groups of very small forms are seen, probably clusters of merozoites derived from recent multiplication by schizogony (fig. 32).

These preparations of the guinea-fowl contain, therefore, taken altogether, all the types of avian blood-parasites with the exception of trypanosomes. Wenyon (1908, p. 141) has, however, described trypanosomes from the guinea-fowl and has named the parasite *Trypanosoma numidæ*. The Leucocytozoon of the guinea-fowl has been named by Balfour *L. neavei*.

The occurrence of Halteridium in this bird has also been noted by Wenyon (l.c., p. 150), but the occurrence of Proteosoma has not, so far as I am aware been recorded; this parasite is, however, so common in birds that there is nothing remarkable in its occurrence in this instance. The Leucocytozoa mostly show the nucleus of the host-cell compact, not drawn out; as already stated, the nucleus of the parasite is not stained. In the Halteridia also the nucleus of the parasite is not to be seen in any of those which I have examined, and is not figured in Lady Bruce's drawings.

(2) *Bee-eater* (*Merops albicollis*??).—There are two slides labelled "bee-eater, 15.11.08." The smears contain trypanosomes, Halteridia, and filariæ.

The trypanosomes are of moderate size (pl. 9, figs. 66, 67), and rather broad forms with the posterior extremity greatly prolonged, so that it simulates a flagellum. The trophonucleus is not far from the kinetonucleus, and between the two is an appearance of a vacuole in some specimens (fig. 67). The flagellum is faintly stained and very difficult to make out even with critical illumination; I am inclined to think that it is longer than is shown in the drawing.

The Halteridia (pl. 8, fig. 33) show coarse pigment-grains, but no nucleus distinctly; I have only been able to make out in some of them red grains, possibly of the nature of chromatin, at the ends of the body.

(3) *Blue Plantain-eater* (*Corytheola cristata*).—There is one slide labelled "Blue Plantain-eater, 6.12.08." The smear contains Halteridia, trypanosomes, and filariæ.

The Halteridia (pl. 8, figs. 34-39) are abundant and of a distinct type, of even thickness, very slightly curved, with coarse

pigment-grains, and with red-staining grains at the two ends of the body in addition to a more diffuse red patch which apparently represents the nucleus and is usually situated near the middle of the body.

The trypanosomes (pl. 9, fig. 68) are scanty and are of a stout fleshy type which has become considerably deformed, apparently, in the process of drying.

(4) *Red-crested Plantain-eater* (*Musophaga rossæ*).—There is one slide labelled “Red-crested Plantain-eater, Kibanga, 8.11.08.” The smear contains abundant Halteridia, of quite a different type from those found in the last bird (pl. 8, figs. 49-52). The parasites are more or less crescent-shaped with pointed ends, often very much bent round the nucleus of the corpuscle. The pigment-grains are not very coarse, and there are no red-staining grains apart from the nucleus which appears as a faintly-stained red patch generally at the middle of the body, sometimes near to one end.

(5) *Francolin* (*Francolinus mulemæ??*).—One slide is labelled “Francolin, 15.12.08.” The corresponding drawing is marked “trypanosomes,” but no trypanosomes are drawn, only Halteridia, Leucocytozoa, and filariæ. The slide shows Halteridia and Leucocytozoa fairly abundantly, but I have not found any trypanosomes.

The Halteridia (pl. 8, figs. 53, 54) are peculiar forms, very vacuolated and with large clumps of coarse pigment-grains, but do not show any signs of chromatin in this preparation. The body stains a purplish colour and grows round the nucleus of the host-cell in such a way that its two opposite ends sometimes almost come into contact.

The Leucocytozoa are large forms showing well-marked male and female types (pl. 9, fig. 70). It is not possible, however, to make out their nucleus clearly.

(6) *Black and White Hornbill* (*Bycanistes subquadratus*).—A slide labelled “Black and white hornbill, 8.11.08,” shows fairly numerous trypanosomes (pl. 9, fig. 69). They are of stout type, with the distinct kinetonucleus placed close to the pointed posterior end of the body; the trophonucleus and the flagellum are very faintly stained and difficult to make out clearly. They are probably deformed to some extent by the process of drying.

(7) *Collar-dove* (*Turtur semitorquata*).—A slide labelled “Collar-dove, 4.1.09,” shows a scanty infection of Leucocytozoa (pl. 9, fig. 71). The parasite has the typical form and appearance. The nucleus of the host-cell is deeply stained and compact, but that of the parasite is indistinct; the cytoplasm of the parasite is very vacuolated.

(8) *Coucal* (*Centropus superciliosus?*).—There are two slides of the coucal, labelled respectively 8.11.08 and 27.11.08. Both slides show a distinct type of Halteridium fairly abundantly (pl. 8, figs. 55-60). The body of the parasite is stout and pale in colour. The pigment-grains are few in number but very coarse.

The nucleus is represented by a faint red patch varying greatly both in shape and position, being sometimes central, sometimes terminal. Double infections of the corpuscles are frequent, and the parasites are seen in various stages of growth.

(9) *Ibis* (*Ibis aethiopica?*).—A slide labelled “Ibis, 1.12.08,” shows an abundant infection of most peculiar Halteridia (pl. 8, figs. 40-48). The bodies of the parasites are very irregular in form, often with peculiar processes resembling pseudopodia; occasionally, however, a compact sausage-like form (fig. 47) is found, perhaps representing a full-grown ripe gametocyte. The pigment-grains are fine and distributed for the most part in clumps at the surface of the body; the nucleus appears to be represented also by red-stained streaks and patches which are placed at the surface of the body. The parasites are in all stages of growth, and in one case I have found what I believe to be a young Halteridium in the act of invading a corpuscle (fig. 48); it is very difficult to be certain that this is not simply an artefact, a deposit or precipitate of the stain or the like, and I give the figure for what it is worth, but I believe that it really does represent a very young parasite.

(10) *Egyptian Goose* (*Chenalopus aegyptiaca*).—One slide labelled “Egyptian goose, 25.1.09,” shows a fairly rich infection of Leucocytozoa. The preparation is somewhat defective and the blood is largely coagulated, having apparently dried too slowly; in consequence many of the Leucocytozoa have rounded themselves off and present appearances similar to that shown in fig. 72, pl. 9.

II. GENERAL REMARKS.

The following is a list of the various types of blood-parasites represented in this collection, with their hosts:—

Hæmogregarines.

Snake (pl. 7, figs. 1-4).

Tortoise (pl. 7, figs. 5-14).

Crocodile (pl. 7, figs. 15-19).

Hæmocystidia.

Lizard (pl. 7, figs. 20-23).

Halteridia.

Guinea-fowl (pl. 8, figs. 24-26).

Bee-eater (pl. 8, fig. 33).

Blue Plantain-eater (pl. 8, figs. 34-39).

Red-crested Plantain-eater (pl. 8, figs. 49-52).

Francolin (pl. 8, figs. 53, 54).

Coucal (pl. 8, figs. 55-60).

Ibis (pl. 8, figs. 40-48).

Proteosomata.

Guinea-fowl (pl. 8, figs. 25 and 27-32).

Leucocytozoa.

Guinea-fowl (pl. 9, fig. 72).

Francolin (pl. 9, fig. 70).

Collar-dove (pl. 9, fig. 71).

Egyptian Goose.

Trypanosomes.

Small Toad (pl. 9, figs. 61-64).

Tortoise (pl. 9, fig. 65).

Bee-eater (pl. 9, figs. 66, 67).

Blue Plantain-eater (pl. 9, fig. 68).

Francolin (?).

Black and White Hornbill (pl. 9, fig. 69).

Filariae.

Bee-eater.

Blue Plantain-eater.

Francolin.

Of these various types of parasites, the Halteridia deserve special mention. Halteridia are known from a very large number of different species of birds, but not much has been done to distinguish the species of the parasites themselves, and they are generally all included under a single specific name *Hæmoproteus danilewskyi*. Only in a few instances have special names, such as *H. noctuæ*, *H. columbæ*, been given to them, and then rather on the unsafe ground of a difference in habitat, than from any difference in the parasites themselves. Wenyon (1908) remarks that Halteridium was met with in a number of birds on the White Nile, and points out that "the parasites differ according to the host, and probably do not all belong to one species." He figures a curious species from the Jabira Crane, and observes that this species differs from the type usually met with in birds, of which he figures two specimens (l.c., pl. XIII., figs. 21, 22), and states that it occurs in various birds, including the common sparrow of the Sudan and the Guinea-fowl; the form figured by Wenyon appears very similar to that occurring in the Guinea-fowl in this collection (pl. 8, fig. 24). I am not aware of any other attempt to distinguish species of Halteridium by morphological characters.*

* Since this Report was sent to the press, I have received a memoir by Dr. J. Burton Cleland and Mr. T. Harvey Johnston, entitled "Descriptions of new Haemoprotozoa from Birds in New South Wales, etc." (Journ. and Proc. Roy. Soc. N.S.W. XLIII., 1909, pp. 75-96, with two plates and two diagrams), in which the authors describe and compare in detail the Halteridia of four species of Australian birds, namely, *Ptilotis chrysops*, *Philemon corniculatus*, *Geocichla lunulata*, and *Meliornis novae-hollandiæ*. Characteristic differences are pointed out between the parasites in each species of bird, and the Halteridia are given in each case distinct specific "labels" derived from the generic name of the host, namely, *H. ptilotis*, *H. philemon*, *H. geocichlae*, and *H. meliornis*, respectively.

As a glance at plate 8 will show, the Halteridia of different species of birds show differences much too striking to be explained as due to differences of technique and preparation, on the one hand, or, on the other hand, to the modifying influence of a different host on the same species of parasite. The Halteridia differ, as can be seen, in form, size, and structural features such as characters of the cytoplasm, distribution of the melanin-pigment and of the chromatin, &c., making all due allowance for differences of age and sex in the Halteridia themselves. I think there can be no doubt that in the future it will become necessary to recognize distinct species of Halteridia characterized by definite structural peculiarities, and not by their habitat, since the same species may often occur, probably, as Wenyon supposes, in several species of birds.

A remarkable feature of these different Halteridia is the great variation seen in their nuclei. The nucleus of this type of parasite stains as a rule very feebly, and many of the preparations show none at all; in other cases the nucleus is visible as a pale pink or reddish patch, showing great differences in size, position, and appearance. Differences in size are probably sexual, when they occur in the same species; some of the appearances exhibited, however, are very peculiar, especially those presented by the Halteridia of the Ibis (pl. 8, figs. 40-48), where the nucleus appears to be represented by a small flattened red patch at the surface of the body. Unfortunately the Romanowsky stain is exceedingly misleading for nuclear structure, and it would not be safe to draw any conclusions from it. In the case of the Halteridium of the Little Owl (*Athene noctua*), preparations made by Woodcock and myself at Rovigno and stained by approved nuclear methods, such as Heidenhain's hæmatoxylin, show the nucleus simply as a round vesicle with a karyosome, just as in a trypanosome; few things are more remarkable or disconcerting than the discrepancy between the results given by the Romanowsky method and other stains.

There is, however, one point to which I may draw attention. A striking feature of the Halteridium of the Blue Plantain-eater (pl. 8, figs. 34-39) is the presence of numerous red-stained grains at the two ends of the body, in addition to a red patch which probably represents the nucleus. The grains occur very abundantly in a young individual, and I have some doubt as to whether they are of the nature of chromatin; the mere fact that they stain red by the Romanowsky method is no proof that they are truly chromatin. But the occurrence of these red-staining grains at the two ends of the body may perhaps explain a very puzzling fact in the literature of Halteridium. Labbé (1894) stated that Halteridium reproduced itself by a process of sporulation at the two ends of the body; he gave figures of Halteridia with small nuclei at the two ends of the body, and of a process of segmentation into merozoites in this region. No one has ever yet confirmed this observation or been able to see anything like it. It seems to me possible that what Labbé mistook for small nuclei at the ends of the body may have been red-staining

grains such as those which are present in the parasite of the Blue Plantain-eater. I may mention that I have also seen similar appearances in Halteridia of the Blue Jay of the Sudan in a preparation made by Major Dansey Browning, R.A.M.C.

Lister Institute,

26th November, 1909.

REFERENCES.

- DUTTON, J. E. and TODD, J. L. (1903). First Report of the Expedition to Senegambia. "Memoir XI., Liverpool School of Tropical Medicine."
- DUTTON, J. E., TODD, J. L., and TOBEY, E. N. (1907). Concerning certain parasitic Protozoa observed in Africa, Part II., "Ann. Trop. Med. Parasitol," I., pp. 287-370, pls. XX.-XXXII., 34 text-figs.
- LABBÉ, A. (1894). Recherches . . . sur les parasites endoglobulaires du sang des vertébrés. "Arch. Zool. Exp. et Gen." (3) II., pp. 55-258, 10 pls.
- LAVERAN, A. and MESNIL, F. (1907). Trypanosomes and Trypanosomiasis. Translated and enlarged by D. NABARRO. London, Baillière, Tindall and Cox.
- RODHAÏN, J. (1908). Note sur quelques trypanosomes de grenouilles et de poissons dans l'Ubanghi. "Centralbl. Bakt. Parasitenkunde, I. Abt. Orig.," XLV., pp. 129-133, 8 text-figs.
- WENYON, C. M. (1908). Report of Travelling Pathologist and Protozoologist. "Third Report of the Wellcome Research Laboratories, Khartoum," pp. 121-168, pls. XII.-XVI.

DESCRIPTION OF THE PLATES.

FIGS. 1-8, 10, 11, 15-19, 27, 33-39, 41-43, 47, 48, 50-53, 56-65, and 68 are drawn by Miss Rhodes at a magnification of 2,000 linear. The remaining figures are drawn by Lady Bruce at a magnification of about 1,650 linear (*see* p. 74).

PLATE 7.

- FIGS. 1-4.—Haemogregarine of a snake (p. 77).
 FIGS. 5-14.—Haemogregarines of a tortoise (p. 77).
 FIGS. 15-19.—Haemogregarines of a crocodile (p. 78).
 FIGS. 20-23.—Haemocystidia of a lizard (p. 76).

PLATE 8.

- FIGS. 24-26.—From blood of "guinea-fowl, 3.1.09" (p. 79); 24, a halteridium; 25, a proteosoma (or a halteridium rounding itself off?); 26, a halteridium (or a proteosoma?) which has escaped from the corpuscle and rounded itself off.
 FIGS. 27-32.—From blood of "guinea-fowl, 15.12.08" (p. 80). Various stages of Proteosoma. 27, very young form; 28-30, older intra-corpuscular forms; 31, schizogony?; 32, free cluster of merozoites.
 FIG. 33.—Halteridium of bee-eater (p. 80).
 FIGS. 34-39.—Halteridia of blue plantain-eater (p. 80).
 FIGS. 40-48.—Halteridia of ibis (p. 82).
 FIGS. 49-52.—Halteridia of red-crested plantain-eater (p. 81).
 FIGS. 53, 54.—Halteridia of francolin (p. 81).
 FIGS. 55-60.—Halteridia of coucal (p. 81).

PLATE 9.

FIGS. 61-64.—Trypanosomes of small toad (p. 74). 61, large form. The striations are only figured on one surface of the body, since it would have confused the drawing had those of both surfaces been drawn, owing to their being nearly parallel on the two surfaces. 62, large form. The striations are figured on both surfaces, in order to show the manner in which they cross each other, owing to the twisting of the body. 63, a portion of the body of a large form showing a small quantity of stain in the nucleus. 64, small form of trypanosome.

FIG. 65.—Trypanosome of tortoise (p. 78).

FIGS. 66, 67.—Trypanosomes of bee-eater (p. 80).

FIG. 68.—Trypanosome of blue plantain-eater (p. 81)

FIG. 69.—Trypanosome of black and white hornbill (p. 81).

FIG. 70.—Leucocytozoon of francolin, male type (p. 81).

FIG. 71.—Leucocytozoon of collar-dove, female type (p. 81).

FIG. 72.—Leucocytozoon of "guinea-fowl, 10.1.09" (p. 80), female type which is in the act of rounding itself off.

39. AMAKEBE: A DISEASE OF CALVES IN UGANDA.

By Colonel Sir DAVID BRUCE, C.B., F.R.S., Army Medical Service; Captains A. E. HAMERTON, D.S.O., and H. R. BATEMAN, Royal Army Medical Corps; and Captain F. P. MACKIE, Indian Medical Service. Sleeping Sickness Commission of the Royal Society, 1908-09.

(Received December 18, 1909,—Read January 20, 1910.)

[PLATE 10.]

Introductory.

Amakebe is the most important disease of cattle in Uganda. It attacks the calves soon after they are born, and destroys more than half of them. Among the native cattle the loss is reported to be as much as 75 per cent., but, with careful nursing and hand-feeding, this mortality may be reduced to between 20 and 30 per cent. This is an enormous toll to pay, and renders the breeding of cattle in Uganda for dairy purposes, or, indeed, for any purpose, very up-hill work.

Little up to the present has been written as to the nature and causation of amakebe. It has been described as a trypanosome disease, but this evidently on insufficient knowledge.

Distribution in Uganda.

Amakebe appears to occur all over the Kingdoms of Uganda, Unyoro, Ankole, and Busoga. Lieutenant A. D. Fraser, Royal Army Medical Corps, the medical officer lately in charge of the Sleeping Sickness Camp, Sesse, reports, however, the curious fact that it does not occur among the cattle on the Sesse Islands. Mr. C. W. Hattersley also informs the Commission that cows brought to Mengo from Ankole invariably contract the disease, which would go to show that in some parts of Ankole the disease does not occur. Mr. R. J. Sturdy, the chief veterinary officer, British East Africa, states that amakebe is found at every altitude in that Protectorate. Dr. A. Theiler, C.M.G., the chief









veterinary bacteriologist, Transvaal, who lately visited Uganda, writes that Dr. Lichtenfeld, the principal veterinary officer, German East Africa, told him that a disease similar to amakebe exists in Ruanda, on the western shores of Victoria Nyanza and adjoining Ankole.

It is evident, then, that this disease is widely prevalent in Central Africa, and most disastrous in its effects.

Nomenclature.

In Uganda the disease is known as kebe, makebe, or amakebe, and means calves' swollen glands, or mumps. At Ngora, to the west of Mount Elgon, the natives call the disease angarwe. In Unyoro, masugu. In Ankole, amashuyu or amashui.

Symptoms.

The chief symptom of this disease is the swelling of the lymphatic glands, especially those in the region of the ear, in front of the shoulder, and in front of the hip. The glands frequently reach a large size, those in front of the shoulder often being three or four inches in length. They are soft to the touch, giving the impression of an elastic body under the skin. The hair is rough and staring, the head hangs, the ears droop, and there is frequently a watery discharge from the eyes and nose. During the illness the temperature runs high, often reaching 107° F. or more. The calf becomes rapidly emaciated, and often a dry scabby eruption of the skin is seen. Diarrhœa is frequent, and the dung is often dark in colour, with an evil odour. The urine never shows any trace of blood, as in redwater.

The duration of the disease is usually about a fortnight, but sometimes the calves get over it in three or four days. The fever goes, they pick up condition, and the swelling of the glands subsides. The glands, however, never regain their normal size, but remain permanently enlarged throughout life.

When a calf has recovered from amakebe it is no longer susceptible to the disease. It is immune for the rest of its life.

The following cases illustrate the course of the disease:—

Experiment 1,387.

To study Amakebe in the Calf.

July 26, 1909.—Animal received from Sir Apolo Kagwa, K.C.M.G., Kampala.

July 29.—The prescapular glands are the size of a walnut. The calf looks fairly well, is thin, and hair slightly rough.

Aug. 2.—The lymphatic glands are much more enlarged. The prescapular glands measure 3½ by 2 inches.

Aug. 12.—This calf is now looking very sick. Conjunctival mucous membrane congested. The hair is falling off in patches, leaving a rough, scabby surface. Diarrhœa.

Aug. 14.—Discharge from eyes and nose. Diarrhœa.

Aug. 26.—This calf got steadily worse, and died at 11.30 a.m. to-day.

The following chart represents the course of the temperature :—

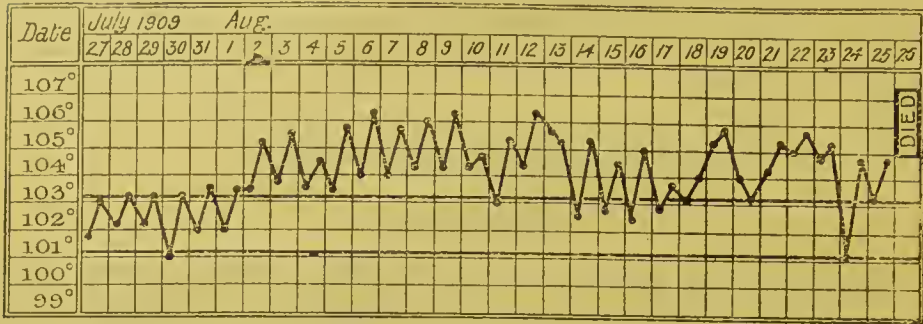


CHART 1.—Experiment 1,387. The Temperature Curve in a severe Case of Amakebe.

Aug. 26, 1909.—*Post-mortem* immediately after death.

External Appearances.—The body is emaciated. *Rigor mortis* absent. The hair is staring and has a ragged appearance. There are many patches of eruption on the surface of the body, especially on the face and head. These eruptions are, as a rule, about the size of half-a-crown and resemble limpet-shells.

Internal Appearances.—On removing the skin, the flesh is seen to be pale in colour. On opening into the abdomen the spleen is seen to be enlarged. The surface of the stomach and intestines is exceedingly pale and yellowish. There is no fluid in the peritoneal cavity. On opening into the thorax no fluid is found in either pleural cavity. There is about a tablespoonful of bright, chrome-coloured, clear fluid in the pericardium. The anterior mediastinum contains a quantity of bright yellow, jelly-like material. The serous membranes are shining and smooth.

Lymphatic Glands.—The lumbar chain of glands are enlarged, some of them being the size of a small walnut. These enlarged glands on being cut into are found to be very œdematous, but not hæmorrhagic. The prescapular glands are much enlarged, being 8 cm. ($3\frac{1}{2}$ inches) in length.

Circulatory System.—*Heart.*—The fat of the auriculo-ventricular groove is infiltrated with gelatinous material, which is bright yellow in colour. There are no petechiæ under the epicardium. On opening into the left ventricle many minute petechiæ are seen under the endocardium. The colour of the aorta is bright yellow. The substance of the heart is pale in colour and flabby to the touch. Weighs 125 grammes ($4\frac{1}{2}$ ounces).

Respiratory System.—*Left lung* is purplish in colour, with a dark purple patch in the anterior lobe about the size of half-a-crown. This, on being cut into, shows hæmorrhagic infarction. On section the left lung appears to be fairly healthy. Weighs 210 grammes ($7\frac{1}{2}$ ounces). *Right Lung.*—Anterior lobe and part of the middle lobe are purplish-red in colour and solid. The anterior lobe sinks in water. The surface is purplish-red in colour, and across the surface is a network of yellow-coloured, clear, jelly-like strands, resembling the lung in a case of horse-sickness. The strands in some places are $\frac{1}{4}$ inch wide. On section the substance is seen to be hepatised and dark purple in colour, and across the cut section the same network of yellow, gelatinous-like material is seen. The posterior lobe is pale in

colour, and on section appears fairly normal. Weighs 345 grammes ($12\frac{1}{4}$ ounces).

Alimentary System.—*Spleen* is enlarged. 29 cm. in length, 9 cm. broad, and 2.5 cm. in thickness ($11'' + 3\frac{1}{2}'' + 1''$). Capsule is purplish in colour. On section the tissue is dark purple in colour and friable. Weighs 245 grammes ($8\frac{3}{4}$ ounces). *Liver* is bright yellow in colour, tinged with red, like bronze. Capsule is smooth. On section the substance is pale, with congested areas. *Gall-bladder* is distended with thick, greenish-yellow bile. Weighs 890 grammes ($31\frac{1}{2}$ ounces).

Fourth Stomach.—Is pale in colour. No ulceration. Intestines not examined.

Urinary System.—*Left kidney.*—Capsule strips readily. On section the cortical part is seen to be pale, with dilated vessels. Weighs 102 grammes ($3\frac{1}{2}$ ounces). *Right kidney*, in a similar condition to the left. Weighs 95 grammes ($3\frac{1}{4}$ ounces).

Experiment 1,634.

To study Amakebe in the Calf.

Sept. 4, 1909.—This calf was brought to Mpumu from Kome, one of the Sesse Islands, and was therefore susceptible to amakebe.

Sept. 14.—Sent into Kampala, in order to become infected.

Sept. 24.—Returned from Kampala.

Oct. 4.—Lymphatic glands much enlarged.

Oct. 18.—Died.

The following chart represents the course of the disease:—

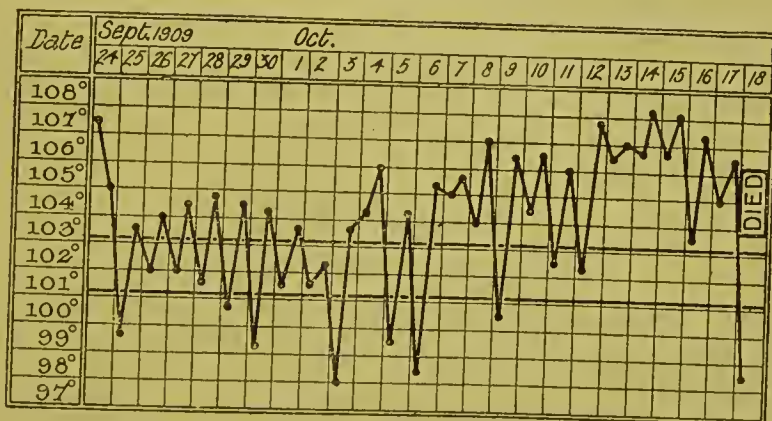


CHART 2.—Experiment 1,634. Temperature Curve in a severe and fatal Case of Amakebe.

Oct. 18, 1909.—*Post-mortem* immediately after death.

External Appearances.—Animal about one year old. Preauricular, prescapular, and precrural glands are much enlarged. The prescapular glands measure 3 inches in length and $1\frac{1}{2}$ inches in breadth. On section the glandular tissue is œdematous and, in some places, hæmorrhagic.

Internal Appearances.—On opening into the peritoneal cavity about a gallon of clear, amber-coloured fluid is found. There is a large quantity of yellow, gelatinous infiltration into the omentum. The serous membrane of the omentum is markedly hæmorrhagic, being covered with small petechiæ. The small intestine is dark crimson in colour and intensely congested. The

whole of the peritoneal aspect of the diaphragm is covered with small hæmorrhages. On removing the sternum a quantity of yellow, gelatinous material is found in the mediastinum. About 2 ounces of the same clear, amber-coloured fluid are seen in the pleural cavity. The pericardium contains a small quantity of clear, straw-coloured serum.

Circulatory System.—Heart.—A quantity of yellow, gelatinous material is seen at the base. Many small petechiæ both inside and outside the heart.

Respiratory System.—A quantity of white frothy fluid exuded from the nose during the last hours of life. On opening into the trachea, however, it is now found to be empty. The *left lung* is partially collapsed and is dark purple in colour. On section the organ is dark crimson in colour and intensely congested. It is, in places, solid in consistence and a portion placed in water sinks. On pressure a white, frothy fluid exudes. *Right lung* is pale in colour, and there are numerous hæmorrhages into the serous membrane. On section it is found to be congested. No part of the lung sinks in water.

Alimentary System.—Spleen is enlarged. Measures 14 inches in length and $4\frac{1}{2}$ inches in breadth. Numerous petechiæ into the capsule. On section the substance is dark in colour, soft, and friable. Weighs 480 grammes (17 ounces). *Liver* is enlarged. On section is seen to be congested. Gall-bladder is distended with dark, olive-green-coloured bile. Weighs 3 lbs. 10 ozs.

Fourth Stomach.—Is reddened, and there are numerous small ulcers in the serous membrane.

Urinary System.—Right Kidney.—Capsule strips readily. There are numerous petechiæ into the capsule. Surface of the organ is injected. On section the kidney is seen to be congested, with many hæmorrhages into the substance. *Left kidney* is in a similar condition to the right.

Experiment 1,636.

To study Amakebe in the Calf.

Sept. 4, 1909.—From Kome. Same history as Experiment 1,634. Great enlargement of lymphatic glands.

Oct. 12.—Died.

The following chart represents the course of the disease:—

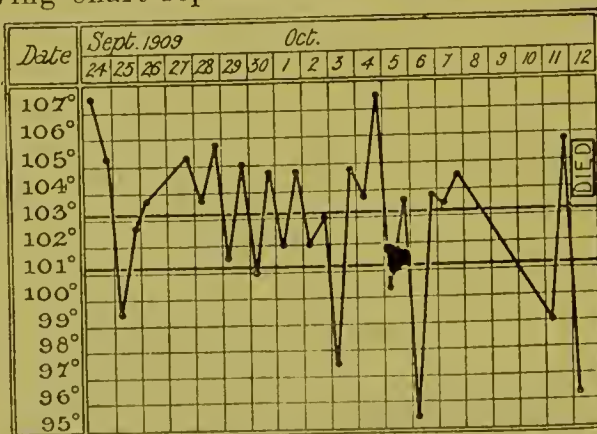


CHART 3.—Experiment 1,636. The Temperature Curve in a severe and fatal Case of Amakebe.

Oet. 12, 1909.—*Post-mortem* two hours after death.

External Appearances.—This calf has had a running from the nose of clear fluid, which has made a small pool under its head, and at death there was a marked collection of white foam at the nose, like that which occurs in horse-sickness, but not to such an extent.

Internal Appearances.—On removing the skin and opening into the peritoneum, about 4 ounces of clear, straw-coloured fluid is found. The omentum is infiltrated with a yellow jelly-like material. On opening into the thorax, 2 ounces of clear, straw-coloured fluid is seen in the pericardium. About 4 ounces of the same straw-coloured fluid in both pleural cavities. On removing the tongue and trachea a large quantity of jelly-like material is found under the trachea.

Lymphatic Glands.—The prescapular glands are enlarged. One measures $4\frac{1}{2}$ inches in length and 1 inch in thickness. On section it is seen to be dark crimson in colour and hæmorrhagic. The glands generally are enlarged and hæmorrhagic. Some of them show signs of breaking down into pus.

Circulatory System.—Heart.—A large quantity of yellow, jelly-like material at the base is seen. There are numerous small petechiæ into the epicardium. None in the endocardium. Muscular substance is pale. Weighs 1 lb. 5 ozs.

Respiratory System.—Tongue normal. The *trachea* is full of white froth. Glands at the bifurcation of the trachea are much enlarged and hæmorrhagic. *Right lung*, anterior lobe is dark purple in colour and is found to be the seat of a large infarct. Posterior lobe is also the seat of an infarct at the margin, about 3 inches by 2 inches in extent. On section the substance of the lung is extremely œdematous. A large amount of frothy fluid exudes on pressure. Weighs 2 lbs. 10 ozs. *Left lung* is also the seat of numerous infarcts. On section a large amount of frothy fluid exudes on pressure. Weighs 1 lb. 6 ozs.

Alimentary System.—Spleen measures 13 inches in length and 4 inches in breadth. On section the substance is soft and friable. Weighs 13 ounces. *Liver* is enlarged. It is full of flukes. The gall-bladder is distended with dark, chocolate-coloured bile, which contains many flukes. Weighs 8 lbs. 5 ozs.

Fourth Stomach.—The mucous membrane of the fourth stomach is congested. It is dark crimson in colour, and numerous small ulcers are seen scattered throughout.

Urinary System.—Right Kidney.—Capsule strips readily. Under the capsule numerous infarcts are seen, about the size of a pea. On section the substance of the organ is congested. Weighs 8 ounces. *Left Kidney.*—Capsule strips readily. In the pelvis of the organ there is a quantity of yellow, jelly-like material. Under the capsule there are also several small infarcts. One of these is as large as a small marble. On section the substance of the kidney is seen to be congested. Weighs 5 ozs.

Experiment 1,386.

To study Amakebe in the Calf.

July 26, 1909.—Received from Sir Apolo Kagwa. Had also been kraaled at Kampala for some days.

Aug. 27.—The course of the disease was much the same as in Experiment 1,387. The prescapular and other glands became much enlarged, one of them measuring 4 inches in length. By this date the calf had recovered, and was returned to owner.

The following chart represents the course of the temperature:—

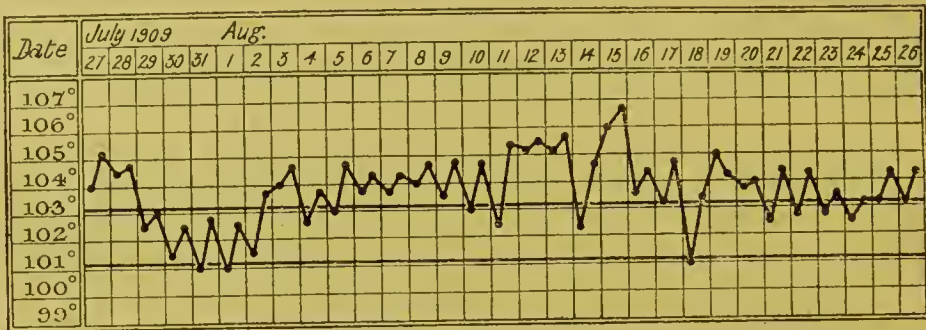


CHART 4.—Experiment 1,386. The Temperature Chart in a Case of Amakebe ending in Recovery.

Experiment 1,635.

To study Amakebe in the Calf.

The following chart represents the course of the temperature:—

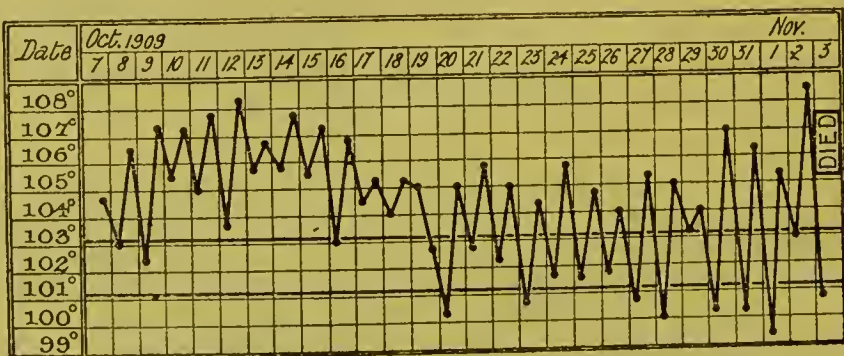


CHART 5.—Experiment 1,635. The Temperature Chart in a Case of Amakebe ending Fatally.

From these foregoing cases and the *post-mortem* examinations, it will be seen that amakebe is an acute disease of calves, and that the main features of the *post-mortem* are signs of intense anæmia, petechiæ of serous membranes, infiltration of jelly-like material into omentum, anterior mediastinum, base of heart, &c., œdema of lungs, swelling and softening of spleen, hæmorrhagic infarcts into lungs, spleen and kidneys, and sometimes ulceration of the mucous membrane of the stomach.

Piroplasms usually Found in the Blood of Uganda Cattle.

When the blood of cattle in Uganda is examined microscopically, two parasites are always to be found, though usually in very small numbers. One of these can readily be recognised as *Piroplasma bigeminum* from its large size and the characteristic appearance of the two pear-shaped bodies (Plate 10, fig. 1). It may, however, also appear as irregularly-shaped, amœboid forms, especially in the spleen (Plate 10, fig. 1). The other parasite is much smaller in size, and is usually seen in the form of a small rod or ring (Plate 10, fig. 2). Both these parasites are inoculable, and appear in the blood of calves without giving rise to any marked disturbance.

Have either of them any connection with amakebe?

The following experiments go to show that they have not:—

Experiment 556.

To ascertain the effect on a Susceptible Calf of the Injection of Blood containing the Small Rod and Ring-shaped Piroplasm. Will it give rise to Amakebe?

February 22nd, 1909.—This calf was born last night. To-day the mother was cleared of ticks by hand-picking, and then completely smeared with a mixture of paraffin and cyllin, and mother and calf then placed in a tick-free enclosure.

February 26th.—Injected this calf with 5 c.c. blood from calf, Experiment 430, whose blood contains the small rod and ring-shaped piroplasm.

The following chart gives the result:—

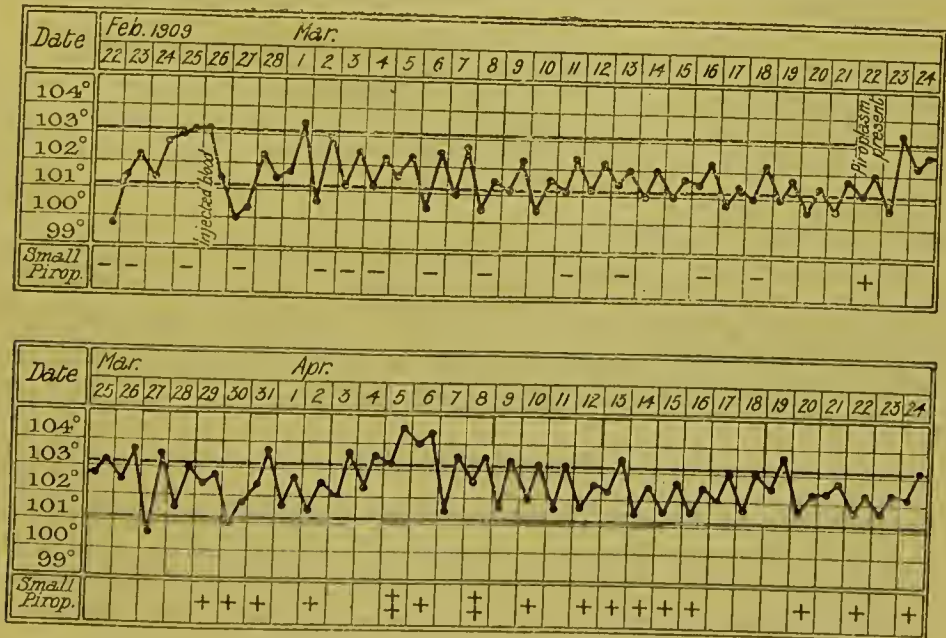


CHART 6.—Experiment 556 represents the Temperature Curve of a Calf which has been Injected with Blood containing the Small Rod and Ring-shaped Piroplasm. The minus and plus signs show the absence or presence of the small rod and ring-shaped piroplasm in the blood.

Remarks.—Twenty-four days after the injection of the blood containing the small piroplasm, the same rod and ring forms appeared in the blood. The temperature curve hardly shows any response to the invasion of the parasite, and the calf shows no signs of illness. It is evident, then, that the injection of blood containing this small piroplasm gives rise to no symptoms like those seen in amakebe.

In the same way the injection of blood containing *Piroplasma bigeminum* is followed, after some days, by the appearance of this parasite.

Experiment 1,901.

To ascertain if the Injection of Blood containing *Piroplasma bigeminum* will give rise to Symptoms of Amakebe.

August 20th, 1909.—Injected 2 c.c. blood containing *Piroplasma bigeminum* into this calf.

The following chart gives the temperature curve:—

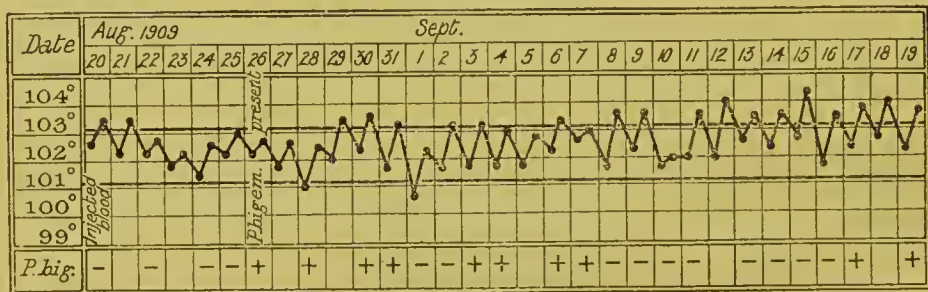


CHART 7.—Experiment 1,901 represents the Temperature Curve of a Calf which has been Injected with Blood containing *Piroplasma bigeminum*. The plus and minus signs show the presence or absence of *Piroplasma bigeminum* in the blood.

Remarks.—Six days after the injection of blood containing the *Piroplasma bigeminum*, this parasite appeared in the blood. The temperature curve is not affected, nor does the calf appear ill. It may, therefore, be concluded that amakebe is not caused by the injection of blood containing either *Piroplasma bigeminum* or the small rod and ring form.

It is well known that *Piroplasma bigeminum* is carried from affected to susceptible animals by different varieties of the blue tick, as well as other species of ticks. It would seem that the small rod and ring form of piroplasm is carried by the brown tick, as the following two experiments will show.

Experiment 747.

To ascertain if Brown Nymphs which had fed as larvæ on an Animal whose blood contained the Small Rod and Ring Forms, are capable of carrying them to a Susceptible Animal, and if the disease so set up will have the Symptoms of Amakebe.

June 24th, 1909.—This calf, like the others, has been brought up in a tick-free shed. It has been under observation since

May 10 without showing any small rod and ring forms in its blood. To-day a large number of brown nymphs, which had fed as larvæ on an ox whose blood contained the small rod and ring piroplasm were placed on this calf. The following chart shows the course of the temperature:—

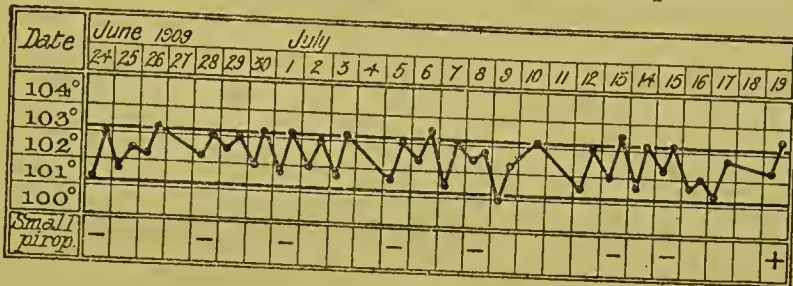


CHART 8.—Experiment 747 represents the Temperature Curve of a Calf upon which Infected Brown Nymphs have been Fed. The *minus* and *plus* signs show the absence or presence of the small rod and ring piroplasm in the blood.

Remarks.—Twenty-five days after the infected brown nymphs were fed on this calf the small rod and ring-shaped piroplasm appeared in the blood. The temperature curve is not affected, and the calf shows no signs of amakebe. It is evident, then, that the small rod and ring-shaped piroplasms transferred to a susceptible calf by means of brown nymphs do not give rise to amakebe.

Experiment 659.

To ascertain if Adult Brown Ticks which had Fed as Nymphs on an Animal whose Blood contained the Small Rod and Ring Forms are capable of carrying them to a Susceptible Animal and setting up the Symptoms of Amakebe.

August 23rd, 1909.—This calf was born on April 4th in a tick-free shed. It has been examined almost daily since that date, and up to the present has shown no parasites of any kind in its blood. To-day a large number of adult brown ticks were placed on this calf.

The following chart shows the course of the temperature:—

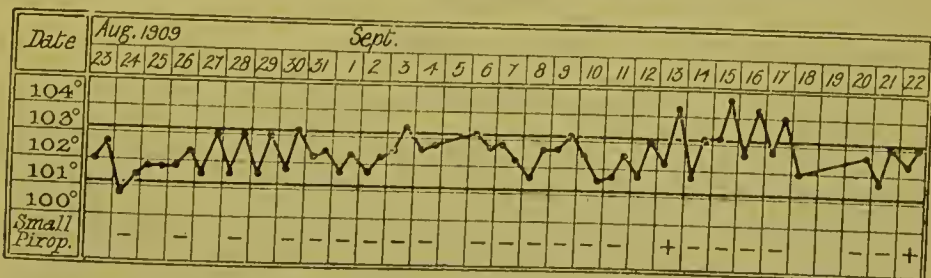


CHART 9.—Experiment 659 represents the Temperature Curve of a Calf upon which Infected Brown Adult Ticks had been Fed. The *minus* and *plus* signs show the absence or presence of the small rod and ring piroplasm in the blood.

Remarks.—Twenty-one days after the infected brown adults had fed on this calf the small piroplasm appeared in the blood.

The temperature curve is only slightly affected, and the calf shows no symptoms of amakebe.

From the foregoing experiments it may be concluded, then, that the appearance of *Piroplasma bigeminum* or of the small rod and ring form of piroplasm in the blood of a susceptible calf, whether introduced by the injection of blood, or in the case of the latter, by the agency of the brown tick, is not accompanied by the symptoms of amakebe. It also is seen from these experiments that the small rod and ring form is inoculable, is carried by the brown tick, and the incubation period is long. This corresponds with the description given by Dr. Theiler, Pretoria, of the piroplasm discovered by him in the Transvaal, and named by him *Piroplasma mutans*.

We may, therefore, consider that the two piroplasms which constantly occur in the blood of Uganda cattle are those known as *Piroplasma bigeminum* and *Piroplasma mutans*, and that neither is the cause of amakebe.

Is Amakebe Inoculable?

It has been shown that blood containing either *Piroplasma bigeminum* or *Piroplasma mutans* if injected into susceptible cattle will give rise to these diseases. Is it equally true that amakebe is inoculable?

The following experiments were carried out to obtain an answer to this question:—

Experiment 1,902.

To ascertain if Blood taken from an Animal suffering from Amakebe and injected into a susceptible Calf will give rise to the Disease.

February 22nd, 1909.—This calf was born last night. Placed in tick-free shed.

February 26th.—Injected with a 5 c.c. blood from calf, Experiment 430, suffering from amakebe.

The following chart shows the result:—

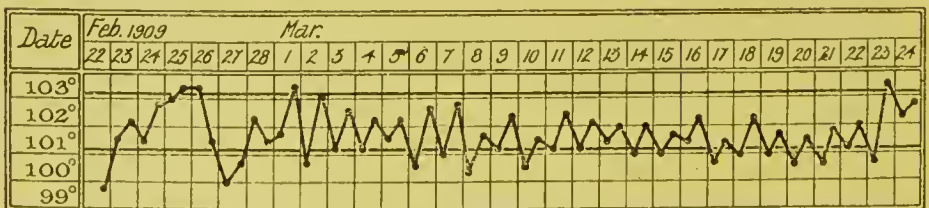


CHART 10 —Experiment 1,902 represents the Temperature Curve of a Calf into which Blood from a Case of Amakebe has been injected.

Remarks.—The temperature curve is not disturbed by the injection of amakebe blood, nor is the calf affected in any way.

Experiment 1,903.

The above experiment repeated.

August 20th, 1909.—Injected 5 c.c. mixture of blood and gland-juice from calf, Experiment 1,387, which is suffering from amakebe.

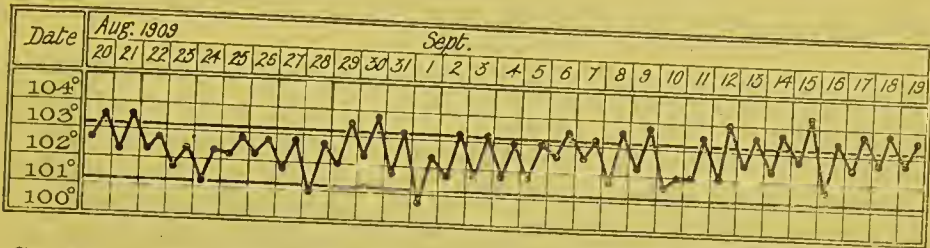


CHART 11.—Experiment 1,903 represents the Temperature Curve of a Calf into which Blood from a Case of Amakebe has been injected.

Remarks.—The result of the injection of amakebe blood is again negative.

Experiment 1,904.

The above experiment again repeated.

August 21st, 1909.—Injected amakebe blood.

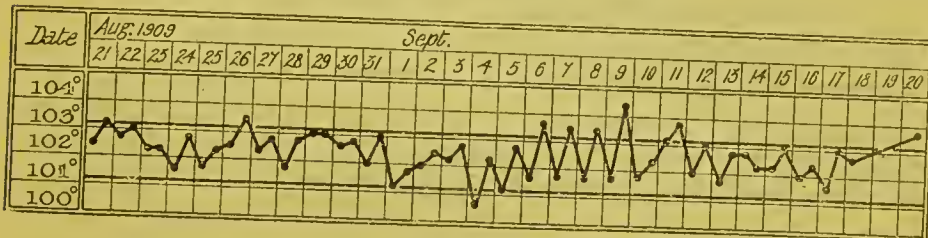


CHART 12.—Experiment 1,904 represents the Temperature Curve of a Calf into which Blood from a Case of Amakebe has been injected.

Remarks.—Result negative.

Experiment 1,905.

September 24th, 1909.—Injected amakebe blood.

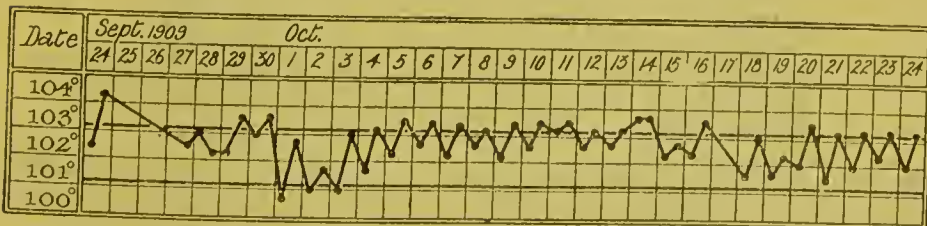


CHART 13.—Experiment 1,905 represents the Temperature Curve of a Calf into which Blood from a Case of Amakebe has been injected.

Remarks.—Result negative.

On three other occasions (Experiments 659, 1,585, and 1,586) was this experiment repeated, and always with a negative result.

It may be concluded, then, that amakebe differs from *Piroplasma bigeminum* and *Piroplasma mutans*, in that it is not inoculable, whereas the latter diseases are.

Result of Exposing Susceptible Calves in a Kraal Contaminated by Amakebe.

Kampala, the native capital of Uganda, has a bad reputation for amakebe. This is probably due to the number of calves stabled in the vicinity. Kampala has a large population of both Europeans and natives, and the milk supply is obtained from private cows kept in the town. The herds of cattle belonging to different individuals are grazed in various parts of the country, but as soon as a cow has calved, she is sent into Kampala to provide milk for her owner. Almost all the calves brought in die of amakebe, which brings about an unhealthy state of things in the cattle kraals where the calves are kept during the day.

The following experiments will show the effect of exposing To ascertain the Effect of exposing a susceptible Calf in a Kraal

Experiment 1,590.

To ascertain the Effect of exposing a susceptible Calf in Kraal contaminated by Amakebe.

October 11th, 1909.—Sent this calf into Kampala.

October 17th.—Returned from Kampala.

The following chart shows the course of the temperature, and the presence or absence of *Piroplasma bigeminum* or the small rod and ring-formed piroplasma in the blood :—

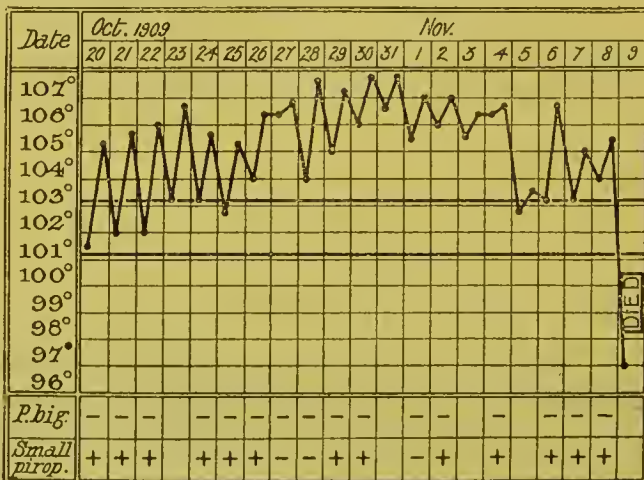


CHART 14.—Experiment 1,590 represents the Temperature Curve of a Calf which has been exposed in a Kraal contaminated by Amakebe. The *plus* and *minus* signs show the presence or absence of *Piroplasma bigeminum* or the small rod and ring piroplasm in the blood.

Remarks.—The result of exposing this calf to a contaminated kraal is an attack of amakebe, characterised by high fever, swollen glands, and death.

Experiment 1,593.

To ascertain the Effect of exposing a susceptible Calf, as in the previous Experiment.

October 11th, 1909.—This calf sent into Kampala.

October 17th.—Returned from Kampala.

The following chart represents the course of the disease, and the presence or absence of *Piroplasma bigeminum* or the small piroplasm in the blood:—

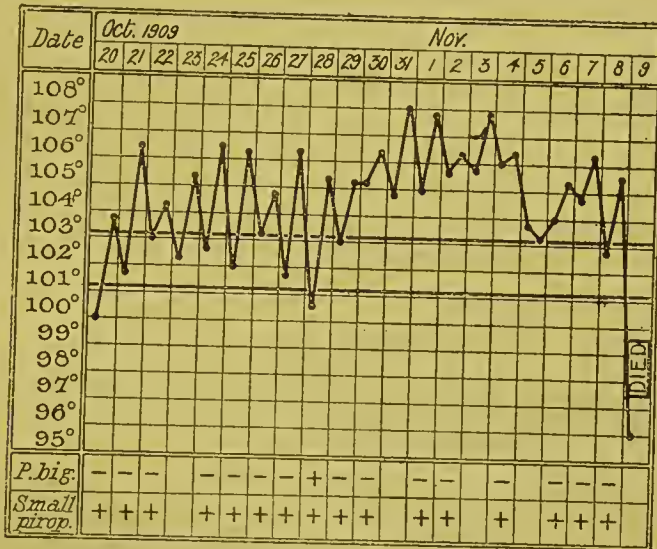


CHART 15.—Experiment 1,593 represents the Temperature Curve of a Calf which has been exposed in a Kraal contaminated by Amakebe. The *plus* and *minus* signs show the presence or absence of *Piroplasma bigeminum* and the small rod and ring piroplasm in the blood.

It is evident, then, that the exposure of susceptible calves for a few days in a kraal where amakebe is common is followed by a serious illness. There is high fever, glandular enlargement, emaciation, and, as a rule, death. This disease has been shown to be caused neither by *Piroplasma bigeminum* nor *Piroplasma mutans*. What, then, is it caused by?

Examination of the Blood in Amakebe.

When the blood of an animal suffering from amakebe is examined, many small piroplasms will be seen (Plate 10, Fig. 3) which appear to be of the same size and shape as *Piroplasma mutans*, and sometimes a few *Piroplasma bigeminum*; otherwise, no new parasite can be said to have come into the blood. This increase in the number of the small piroplasms in the blood of a calf suffering from amakebe, may be explained by saying that the severe illness has led to an excessive multiplication of the *Piroplasma mutans* which was already in the blood. Or, on the other hand, it may be that another species of piroplasm, similar

in size and shape to *Piroplasma mutans*, has appeared in the blood, and that the phenomena of amakebe are due to it.

Marginal Points.—Besides the large and small piroplasms, another kind of body is found in the red blood corpuscles, which Theiler has called *marginal points*. In a lecture delivered by him in August, 1909, at Nairobi, in British East Africa, and published in the "Agricultural Journal of British East Africa," October, 1909, he states: "I have recently come to the conclusion that the disease called gall-sickness, and hitherto looked on as a sequel of redwater, is due to the presence of another parasite, which I have called 'Marginal Points' owing to their position in the red blood corpuscles. Gall-sickness is, therefore, a separate and distinct disease." Dr. Theiler considers it proved that this new disease is transmitted by the blue tick. This all shows how complicated and difficult to distinguish are the diseases of cattle. An ox may have *Piroplasma bigeminum*, small rod and ring-shaped piroplasms, marginal points, and one or two species of trypanosome in its blood at the same time. To which parasite have the different phenomena of the disease to be credited?

The two following tables give the blood examination in two cases of amakebe, and illustrate this complexity:—

Experiment 1,387.—Blood Examination in a Case of Amakebe.

Date.				Parasites in Blood.			No. of Red Blood Corpuscles in 1 c. mm. of Blood. Normal 10,000,000.
				<i>Piroplasma bigeminum</i> .	Small Rod and Ring Forms.	Marginal Points.	
1909.							
July	28	—	—	+	
"	29	—	+	—	
"	30	—	—	+	
"	31	—	—	+	
August	1	—	—	—	
"	2	—	—	++	5,420,000
"	3	—	+	++	5,670,000
"	4	—	+	—	
"	5	—	—	+	
"	6	—	+	++	5,680,000
"	7	—	+	++	
"	8	—	+	+	
"	9	—	+	+	
"	10	—	—	+	
"	11	—	—	++	4,420,000
"	13	—	+	+++	
"	14	—	+	+++	
"	16	—	—	+++	4,540,000
"	19	—	+	+++	4,500,000
"	23				2,890,000
"	24	+++	+	+	2,820,000

Table I., Experiment 1,387. The parasites to be found in a case of amakebe. The *plus* and *minus* signs show the presence or absence of these bodies in the blood. The fourth column gives the number of red blood corpuscles in a cubic millimetre. + present, ++ numerous, +++ very numerous.

Experiment 1,636.—Blood Examination in a Case of Amakebe.

Date.	Parasites in Blood.			
	<i>Piroplasma bigeminum.</i>	Small Rod and Ring Forms.	Marginal Points.	<i>Trypanosoma vivax.</i>
1909.				
September 24 ...	—	—	—	—
" 27 ...	+	+	+	—
" 28 ...	—	+	—	—
" 29 ...	—	—	—	—
" 30 ...	—	—	—	—
October 1 ...	—	—	—	+
" 2 ...	+	+	—	—
" 4 ...	—	—	—	—
" 5 ...	—	+	—	—
" 6 ...	—	++	—	—
" 7 ...	—	+	+	—
" 8 ...	—	+	—	+
" 9 ...	—	+	+	+
" 11 ...	+	+	+	+
" 12 ...	+	+	+	+

Table II., Experiment 1,636. Parasites found in a case of amakebe. The *plus* and *minus* signs show the presence or absence of these bodies in the blood.

Remarks.—From these two tables it will be seen that small piroplasms and marginal points are commonly found in amakebe, and that trypanosomes may also be present.

The marginal points are small, deeply-staining bodies, usually placed near the edge of a red blood corpuscle (Plate 10, Fig. 3). If these bodies really constitute a new and undescribed parasite, the discovery will be one of the greatest interest. Bodies similar in every way to these are found, however, in healthy young rats, goats, calves, &c., so that it is difficult to believe at once in their parasitic nature. Rather would they appear to be cell enclosures, due to rapid changes taking place in the blood, such as take place in young animals or in anæmias. In amakebe they are sometimes very numerous, and it requires no great stretch of the imagination to see in them the youngest stage of the intra-corpuscular parasite, which from being round becomes wedge-shaped, oval, or circular, and rod-shaped. It may be that both these views are true—that some of the so-called marginal points are remains of chromatin from some previous nuclear structure, and that others are the earliest stages of an intra-corpuscular parasite. More work is required before any definite conclusion can be arrived at.

Koch's Granules or Blue Bodies.—Another body which may sometimes, though rarely, be seen in the blood of amakebe calves, is one similar to that first described by Koch, and known as Koch's Granules or Blue Bodies. They are found principally in the spleen, lymphatic glands and liver, where they may be

quite numerous. Stained by Giemsa the body appears as a blue-coloured cell, filled with coarse chromatin granules (Plate 10, Fig. 5).

The following table gives cases of amakebe in which these bodies were found:—

Experiment.	Date.	Spleen.	Liver.	Lymphatic Glands.	Kidney.	Lung.	Blood.
	1909.						
415	May 10	...	+				
1392	July 24	...	+				
1593	Nov. 10	...	+				
1633	Oct. 5	...	+++	+++			
1634	" 18	...	++	+	+	+	
1635	" 15	...					+
1636	" 12	...	+	+	+	+	
1637	" 6	...	+	+	+	+	
1638	" 6	...	++	++	+	+	+
1833	—	...	+	+	+		
1888	Nov. 5	...	++				
1891	" 8	...	+				
1908	" 14	...	++				

Table III., showing the presence of blue bodies in cases of amakebe. + present, + + numerous, + + + very numerous, — absent.

Diagnosis of Amakebe.

What, then, is amakebe? In the opinion of the Commission it is the disease of cattle discovered by Koch, and named by him East Coast Fever. The chief ground for this opinion are, the symptoms during life, the appearances after death, the occurrence of a small piroplasm in the blood indistinguishable from *Piroplasma parvum*, and lastly and chiefly, the presence of the blue bodies in the spleen and other organs. These bodies have never been known to occur in any other disease, and the diagnosis of East Coast fever is made in South Africa if such bodies are found in spleen smears.

Conclusions.

1. The blood of cattle in Uganda almost always contains *Piroplasma bigeminum* and *Piroplasma mutans*, and the cattle are therefore immune to these two diseases.

2. The disease of calves called amakebe is East Coast fever, so that very many of the cattle in Uganda are almost immune to this disease.

3. Owing to the nature of East Coast fever, inasmuch as animals recovered from the disease are no longer infective, some calves may escape attack of amakebe, and so remain susceptible.

4. Thus the calves of the Sesse Islands escape amakebe, and when as grown-up cattle they are transferred to the mainland, they mostly die of East Coast fever.

5. The carriers of East Coast fever—*Rhipicephalus appendiculatus*, or brown tick; *Rhipicephalus evertsi*, or red-legged tick; and *Rhipicephalus simus*—are all common in Uganda.

DESCRIPTION OF PLATE 10.

FIG. 1.—The two upper corpuscles show the characteristic pear-shaped forms of *Piroplasma bigeminum* as they appear in the blood. The lower amceboid forms are drawn from a preparation of spleen. Stained Giemsa. $\times 2000$.

FIG. 2.—*Piroplasma mutans* in the blood. Stained Giemsa. $\times 2000$.

FIG. 3.—The small rod and ring-shaped piroplasm, as seen in the blood of a case of amakebe. Among them are the deeply-stained bodies known as marginal points. Stained Leishman. $\times 2000$.

FIG. 4.—Red blood corpuscles containing piroplasms from the spleen of a case of amakebe. Stained Giemsa. $\times 2000$.

FIG. 5.—Koch's granules or blue bodies from the spleen of a case of amakebe. Stained Giemsa. $\times 2000$.

THE
LIBRARY
OF THE
MUSEUM OF
COMPARATIVE ZOOLOGY
AT HARVARD UNIVERSITY

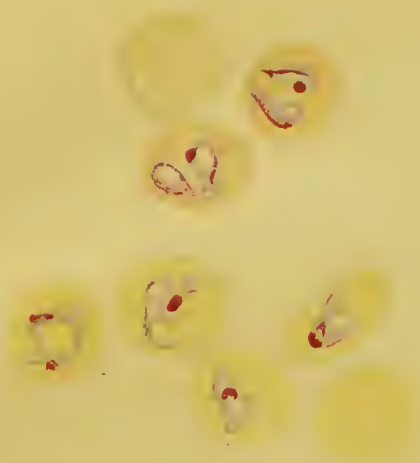


Fig. 1.

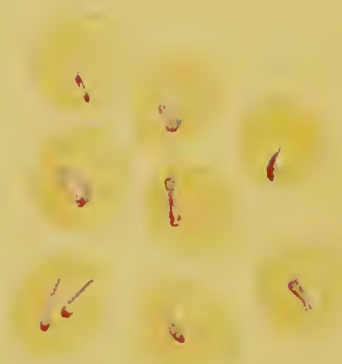


Fig. 2.

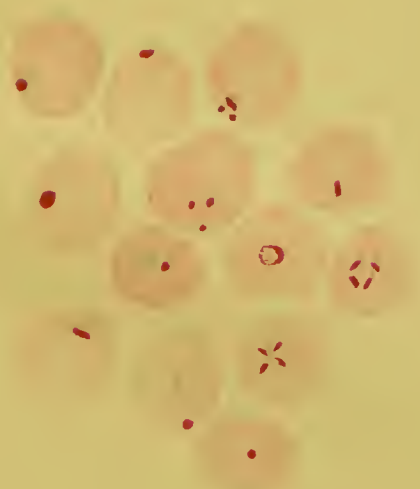


Fig. 3.



Fig. 4.

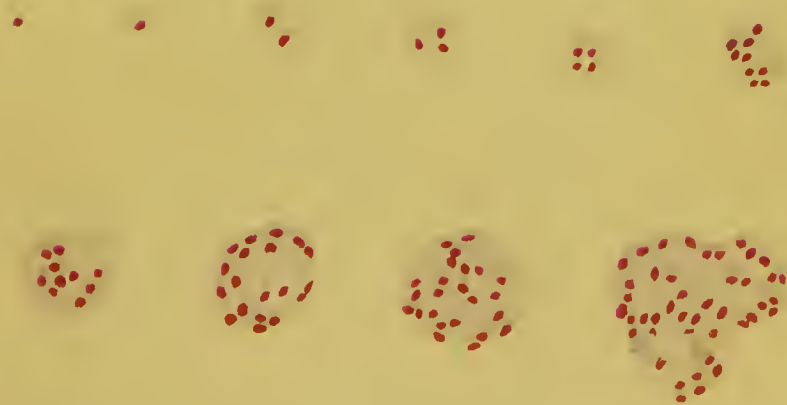


Fig 5.

